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Cardiovascular health status and its associations with cardiovascular disease and ischemic heart disease prevalence in Australian adults

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Abstract

Background

Cardiovascular disease (CVD) and ischemic heart disease (IHD) are two major health burdens. It has been suggested that the improvement of modifiable lifestyle factors could substantially reduce the CVD and IHD risk. To define and monitor the cardiovascular health (CVH) status in the general population, the American Heart Association has outlined seven modifiable lifestyle-related factors [smoking, body mass index (BMI), physical activity, dietary pattern, total cholesterol (TC), blood pressure (BP), and fasting plasma glucose (FPG)] and they were also called Life's Simple 7. A number of studies have measured the CVH status and explored its association with CVD/IHD risk. However, very few studies have used Life's Simple 7 in Australian adults.

Methods

Firstly, we conducted two systematic reviews to estimate the CVH status and explore the association between the CVH status and CVD/IHD related events in adults worldwide. We searched PubMed, Embase, and the Cochrane Central Register of Controlled Trials and relevant articles published between 2010 and 2018.

Secondly, we used the core sample of the 2011-2012 Australian Health Survey and included 7499 adults (≥ 18 years) with available TC and FPG tests. We estimated the proportions of ideal status for the seven CVH metrics and the prevalence of overall poor (having 0-2 ideal CVH metrics) and ideal (having 5-7 ideal CVH metrics) CVH status in the overall Australians and sex/age subpopulations. In addition, we explored the associations between the ideal status of individual metrics, using Poisson regression analysis and population attributable fractions, and overall CVH status, using logistic regression analysis, on the CVD and IHD prevalence in the overall Australians and sex/age subpopulations.

Results

The first systematic review indicated that FPG has the highest proportion of ideal status (69.1%) whereas the dietary pattern has the lowest (12.1%) for adults worldwide. 32.2% and 19.6% of adults have overall poor and ideal CVH status. Compared to males and older adults (≥ 60 years), females and younger adults (< 60 years) have lower proportions of the overall poor CVH status and higher proportions of ideal status for most CVH metrics and the overall ideal CVH status. The CVH status has improved over study time and there may exist regional variations in CVH status. The second systematic review suggested that a higher number of ideal CVH metrics was associated with a

reduced risk of CVD-related events. The separate effects of ideal metrics on CVD risk were inconsistent. Very few studies have explored the sex and age variations in the magnitude of associations between CVH status and CVD/IHD risk.

Among Australian adults, the ideal status was highest for FPG (83.6%) and was lowest for dietary pattern (4.8%). 39.85% and 18.72% of adults were having overall poor and ideal status, respectively. Females and younger adults (18-39 years) have better CVH status, in terms of proportions of ideal metrics and the overall CVH status, in comparison to that in males, middle-aged (40-59 years), and older adults (≥ 60 years). We noticed that smoking, high BMI, elevated BP, elevated TC, elevated FPG, and physical inactivity were significant CVD risk factors and contributors in Australian adults. Physical inactivity, high BMI, and elevated TC were found to be significant IHD risk factors and contributors. The higher number of ideal metrics was associated with a substantial reduction in CVD and IHD prevalence in Australian adults. Our findings illustrated the possible sex and age disparities in the strengths of association between the CVH status and CVD/IHD prevalence.

Conclusions

The thesis indicated that the CVH status was poor for adults worldwide and in Australia, and the proportion of ideal status was especially low for some metrics, such as dietary pattern. The higher number of ideal CVH metrics was associated with a lower risk of CVD and IHD. There existed some sex and age disparities in the CVH status and its association with CVD/IHD risk. More studies are needed to carry out population-based strategies to monitor and improve the CVH status in adults from worldwide and Australia.

Declaration by author

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including statistical assistance, survey design, data analysis, significant technical procedures, professional editorial advice, financial support and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my higher degree by research candidature and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

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Publications included in this thesis

1. **Peng Y**, Cao S, Yao Z, Wang Z. *Prevalence of the cardiovascular health status in adults: a systematic review and meta-analysis*. Nutrition, Metabolism and Cardiovascular Diseases 2018; 28(12): 1197-1207. doi: 10.1016/j.numecd.2018.08.002. – incorporated as Chapter 2.

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2. **Peng Y,** Dong B, Wang Z. *Overall and Gender-specific Associations between C-reactive Protein and Stroke Occurrence: A Cross-sectional Study in US*. Journal of Stroke 2016; 18(3): 355-357. doi: 10.5853/jos.2016.00451.

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4. Dong B, **Peng Y**, Wang Z, Adegbija O, Hu J, Ma J, Ma Y. *Joint association between body fat and its distribution with all-cause mortality: A data linkage cohort study based on NHANES (1988-2011).* PLoS One 2018; 13(2): e0193368. doi: 10.1371/journal.pone.0193368.

5. Wang Z, **Peng Y**, Liu M. *Age Variation in the Association Between Obesity and Mortality in Adults*. Obesity 2017; 25(12): 2137-2141. doi: 10.1002/oby.21976.

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Contributions by others to the thesis

No contributions by others.

Statement of parts of the thesis submitted to qualify for the award of another degree

No works submitted towards another degree have been included in this thesis.

Research Involving Human or Animal Subjects

The ethics approvals were obtained from UQ School of Medicine Low Risk Ethical Review Committee (approval number 2016-SOMLRE-0161) and University of Queensland Medicine, Low & Negligible Risk Ethics Sub-Committee (approval number 2018000244).

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Keywords

cardiovascular health, Life’s Simple 7, Australian adults, cardiovascular disease, ischemic heart disease

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List of Abbreviations used in the thesis

ABS – Australian Bureau of Statistics

AF – atrial fibrillation

AHA – American Heart Association

AHS – Australian Health Survey

BMI – body mass index

BP – blood pressure

CHD – coronary heart disease

CI – confidence interval

CVD − cardiovascular disease

CVH – cardiovascular health

FPG – fasting plasma glucose

HF – heart failure

ICAS – intracranial artery stenosis

ICD – International Classification of Diseases

IHD – ischemic heart disease

IRR – incidence rate ratio

MI – myocardial infarction

NHANES – National Health and Nutrition Examination Survey

NHMS – National Health Measures Survey

NHS – National Health Survey

NNPAS – National Nutrition and Physical Activity Survey

NOS – Newcastle-Ottawa Scale

OR – odds ratio

PAF – population attributable fraction

RADL – Remote Access Data Laboratory

RR – rate ratio

TC – total cholesterol

VTE – venous thromboembolism

YLL – years of life lost

Chapter 1 – Introduction

Background

Cardiovascular disease (CVD) is still one of the leading causes of health burden worldwide. According to the Global Burden of Disease Study, CVD contributed to 17.6 million deaths in 2016, which accounted for nearly 32.3% of all deaths. [1] Ischemic heart disease (IHD), another term of coronary heart disease (CHD), is the most prevalent type of CVD and it contributed to 9.5 million deaths globally in 2016. [1] Both CVD and IHD are also major health concerns for Australians. CVD attributed to over 46 thousand deaths, over 30% of all deaths, among Australians in 2009 [2] and another large-scale study reported that 22% Australians aged 45 or over have a prior history of CVD. [3] The 2016 Global Burden of Disease Study listed IHD as the largest causes of deaths in Australia. [1]

There is a growing body of evidence indicated that the separate and combined effects of modifiable lifestyle factors could explain a large proportion of CVD and IHD cases. A recent meta-analysis indicated that current smoking, physical inactivity, and raised body mass index (BMI) were all independently associated with higher risk of CHD incidence and CVD mortality. [4] A Chinese cohort study revealed that 67.9% of major coronary events could be prevented if participants adhered to six lifestyle-related metrics, including optimal status of smoking, alcohol consumption, physical activity, dietary pattern, BMI, and waist-to-hip ratio. [5] Similarly, a cohort study suggested that approximately 73% of CHD cases were attributable to poor adherence to six lifestyle factors. [6]

Given the enormous global public health burden of CVD and IHD, the American Heart Association (AHA) has worked out the 2020 Impact Goals as follows: "By 2020, to improve the cardiovascular health (CVH) of all Americans by 20% while reducing deaths from CVD and stroke by 20%". [7] Meanwhile, the AHA also outlined seven modifiable metrics, including non-smoking, BMI, physical activity, dietary pattern, total cholesterol (TC), blood pressure (BP), and fasting plasma glucose (FPG), to define and monitor the CVH status in the general population. [7] These CVH metrics were also called Life's Simple 7. There are also other wide-used tools to explore the lifestyle factors and risk of CVD or IHD, such as Framingham risk score [8, 9] and absolute cardiovascular risk assessment.[10] The AHA's Life's Simple 7 has its benefits over those metrics. Life's Simple 7 aimed to measure the CVH and improve the distribution of CVD risk factors in the whole population. It corresponded to the primordial prevention of CVD in the general population. However, the other metrics aimed to identifying a small proportion of population with high risk of CVD, and they reflected the primary prevention of CVD in the high-risk population. As it is widely recognized that the majority of CVD events occur in individuals with average or only mildly adverse levels of risk factors, [7] the Life's Simple 7 could more effectively reduce the CVD burden in the whole population when compared to other metrics. Another advantage of Life's Simple 7 is it contained more CVD risk factors, like dietary pattern, and it is more easily to measure in the population.

Given the advantages of Life's Simple 7, a number of studies have used Life's Simple 7 to measure the CVH status in the general population [11, 12] and explored its association with CVD/IHD risk. [13, 14] Most studies implied the low prevalence of the ideal CVH status in the general population and indicated the significant separate and combined effects of the CVH status on CVD/IHD risk. However, the CVH status was still unclear for adults globally and strengths of association between the CVH status and CVD, including IHD, risk is inconclusive. Additionally, very few studies have used the Life's Simple 7 to evaluate the CVH status in Australian adults and explored its association with CVD/IHD risk. Furthermore, several studies have indicated that there existed sex and age variations in the CVH status and its magnitude of association with CVD/IHD risk while the findings are inconclusive. [15-18]

Our study conducted two systematic reviews and three original research studies, based on a nationally representative Australian survey, to fill those knowledge gaps.

Research aims and objectives

Our study aims to estimate the CVH status and explore its association with both CVD and IHD prevalence in Australian adults. Our findings could provide evidence to the policy makers in order to prioritize the CVD and IHD prevention strategies.

The objectives of the thesis are as follows:

(1) To evaluate the CVH status in adults worldwide.
(2) To summarize findings on the association between the CVH status and risk of CVD, including IHD, in adults worldwide.
(3) To examine the CVH status in Australian adults.
(4) To clarify the association between the CVH status and CVD prevalence in Australian adults.
(5) To illustrate the association between the CVH status and IHD prevalence in Australian adults.

Structure of the thesis

The thesis consisted of seven chapters and they were shown in **Figure 1.1**.

Chapter 1 is a general introduction of the PhD thesis, including background, research objectives, and structure.

Chapter 2 is a systematic review and meta-analysis, aiming to describe the CVH status in adults globally. This study calculated the pooled ideal prevalence of the seven CVH metrics and the proportions of overall ideal and poor CVH status, which were defined by the number of ideal CVH metrics, in adults worldwide. It also conducted subgroups analyses on sex, age, continents, and study periods.

Chapter 3 is a systematic review to summarize the findings on the effects of Life's Simple 7 on CVD/IHD risk in adults worldwide. It examined the effects of individual metrics and the overall CVH status on CVD/IHD risk. It also included stratification analyses on sex and age.

Chapter 4 is an original research study on the CVH status of Australian adults using the core sample of the 2011-2012 Australian Health Survey (AHS). It described both the prevalence of the ideal CVH metrics and the proportions of overall poor and ideal CVH status and stratified by sex and age.

Chapter 5 is an original research study on the association between the CVH status and CVD prevalence among Australian adults using the core sample of the 2011-2012 AHS. It examined the associations between individual metrics and the overall CVH status on CVD prevalence and stratified by sex and age.

Chapter 6 is an original research study on the association between the CVH status and IHD prevalence among Australian adults using the core sample of the 2011-2012 AHS. It examined the associations between individual metrics and the overall CVH status on IHD prevalence and stratified by sex and age.

Chapter 7 summarised the findings of the thesis, discussed the implications of the findings, listed the strengths and limitations, and suggested future research directions.

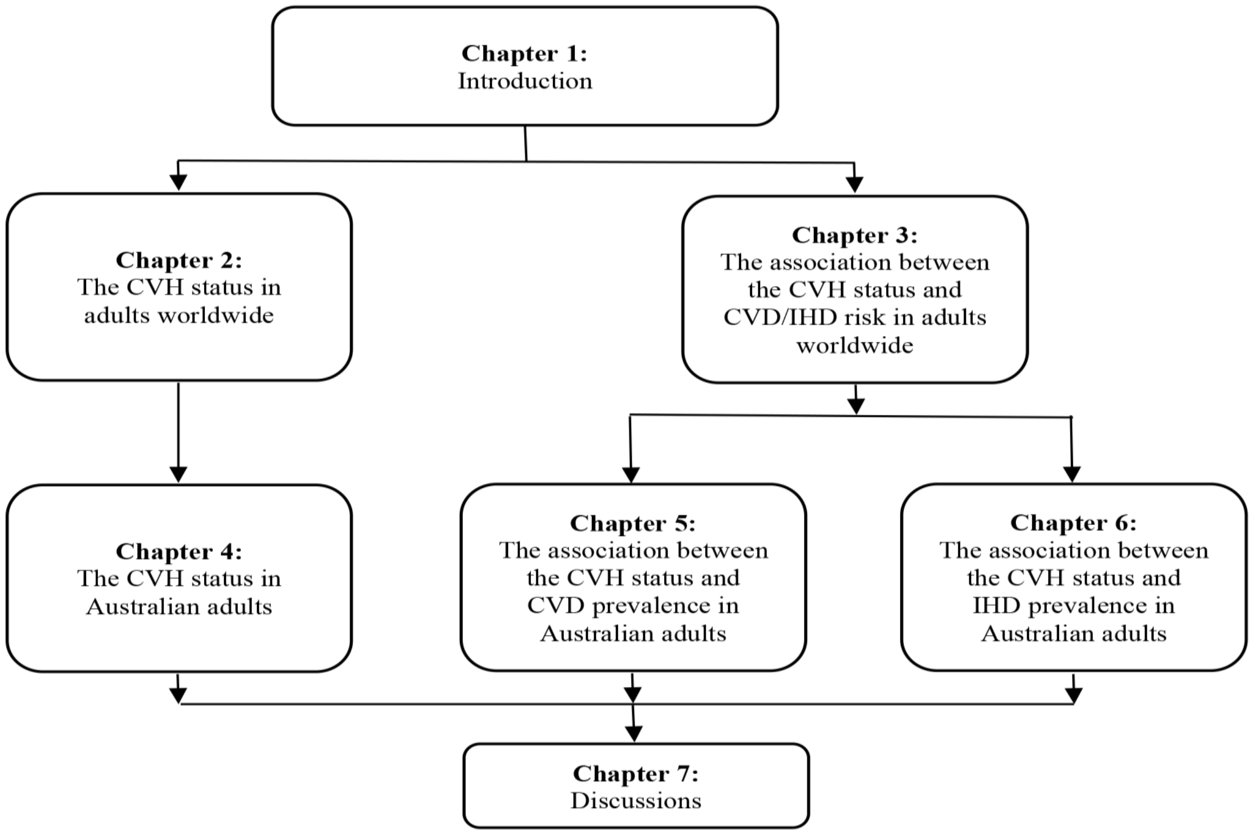

Figure 1.1 Structure of thesis.

Chapter 2 – The CVH status in adults worldwide

The AHA released a guideline to define and monitor the CVH status in the general population while the global CVH status in adults was still unclear. In addition, the sex, age, continent, and study period variations in the CVH status were inconclusive. Understanding the global CVH in adults is crucial for prioritising the public health strategies for CVD prevention. This chapter summarized the findings from relevant studies using a systematic review and meta-analysis and it addressed the research objective 1 of the thesis.

This chapter was formatted as the following publication:

Peng Y, Cao S, Yao Z, Wang Z. *Prevalence of the cardiovascular health status in adults: a systematic review and meta-analysis*. Nutrition, Metabolism and Cardiovascular Diseases 2018; 28 (12): 1197-1207. doi: 10.1016/j.numecd.2018.08.002.

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Yang Peng (Candidate)	Conception and design (80%) Data analysis and result interpretation (50%) Drafting of article (100%)
Sifan Cao	Data analysis and result interpretation (30%) Reviewing of article (30%)
Zhenjiang Yao	Data analysis and result interpretation (20%) Reviewing of article (30%)
Zhiqiang Wang	Conception and design (20%) Reviewing of article (40%)

Prevalence of the cardiovascular health status in adults: a systematic review and meta-analysis

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Abstract

Background and Aims: The AHA has outlined seven CVH metrics, including smoking, BMI, physical activity, dietary pattern, TC, and FPG, to define and monitor the CVH status. Our study was to evaluate the global CVH in adults.

Methods and Results: We searched PubMed, Embase, the Cochrane Central Register of Controlled Trials, and reference lists of relevant articles for studies published between 1 January 2010 and 30 June 2018. Included studies should report the proportions of ideal status for the seven CVH metrics and/or provide the prevalence of overall poor (having 0-2 ideal metrics) or ideal (having 5-7 ideal metrics) CVH status in adults. 88 articles were identified: 75 for the prevalence of ideal CVH metrics, 58 for the proportion of the overall poor CVH status, and 55 for the proportion of the overall ideal CVH status. Smoking had the highest prevalence of ideal status (69.1%) while dietary pattern has the lowest (12.1%). 32.2% and 19.6% of participants had overall poor and ideal CVH, respectively. Females and young adults had better CVH status when compared to males and older adults. There existed regional variations in the ideal CVH metrics and the overall CVH status. The overall CVH status had improved over study time.

Conclusion: The prevalence of ideal status was low for some metrics, such as dietary pattern, and the overall CVH status was still unsatisfactory. We should continue to measure the CVH status and carry out lifestyle interventions to improve the CVH status in the whole population.

Keywords: Cardiovascular health; Adults; Meta-analysis

Introduction

CVD is still the leading cause of health burden worldwide. A recent report confirmed that CVD contributed to 31.5% of the overall deaths globally in the year of 2013. [19] According to the 2011-2014 National Health and Nutrition Examination Survey (NHANES), an estimated of 92.1 million US adults are suffering from CVD. [20] While a large proportion of CVD can be prevented by adhering to healthy lifestyle factors. In a US cohort study with nearly 90 thousand participants and a 20 years' follow-up duration, poor adherence to six lifestyle factors, including smoking, raised BMI, insufficient physical activity, long time television watching, unhealthy diet, and elevated alcohol consumption, explained 73% of CHD cases. [6] Similarly, a Chinese cohort indicated that 68% of the major coronary events were attributed to poor adherence to healthy lifestyle. [5]

In the context of the alarming situation, the AHA has set the strategic impact goal for 2020. It aimed to reduce deaths from CVD and stroke by 20% while improving the CVH of all Americans by 20%. [7] Meanwhile, the AHA identified seven CVH behaviors and factors [smoking, BMI, physical activity, dietary pattern, TC, BP, and FPG] to define and monitor the CVH status. [7] According to AHA's 2018 heart disease and stroke statistics update, the prevalence of ideal status, among US adults, was 77.1% for smoking, 60.3% for TC, 53.2% for FPG, 49.7% for physical activity, 45.4% for BP, 29.6% for BMI, and 1.1% for dietary pattern. [21] Over the past several years, there have been numerous studies applied the AHA's guideline and examined the CVH status within and outside of the US, whereas the global CVH status is still unclear. Although a systematic review has summarized findings of those published on or before July 2015, it failed to provide the pooled proportions of the ideal CVH metrics as well as the pooled prevalence of the overall poor or ideal CVH status. [11] It also failed to examine the possible sex, age, and regional differences as well as the secular trend in the CVH status. Additionally, several studies have been published since July 2015 and, thus, a reassessment of the topic could provide the policy makers with the up-to-date information on this issue.

In this study, we aimed to synthesize data on the prevalence of ideal CVH metrics and evaluate the frequency of the overall ideal and poor CVH worldwide. We also examined the age, sex, geographical, and study period variations.

Methods

Data collection and extraction

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-analyses Of Observational Studies in Epidemiology guidelines. [22, 23] Since the AHA's statement was released in early 2010, we searched relevant studies published between 1 January 2010 and 30 June 2018, by searching PubMed, Embase, and the Cochrane Central Register of Controlled Trials. **Table 2.1** provided the detailed search strategies. In addition, we manually reviewed the reference lists of the included studies. There were no language restrictions. This systematic review was registered in the PROSPERO (registration number: CRD 42017080678). The study outcomes included prevalence of ideal status of the seven CVH metrics and the proportions of overall poor and ideal CVH status. Participants who had 0–2, 3–4 and 5–7 CVH metrics at the ideal level were defined as having overall poor, intermediate and ideal CVH status, respectively. To be included, the studies should satisfy all of the following criteria: (a) cross-sectional or cohort studies; (b) measured seven metrics outlined by AHA; (c) reported proportions of the ideal status for the seven metrics or proportions of the overall ideal or poor CVH status; and (d) all the participants were 18 years or older. The AHA's definitions of ideal status for the seven metrics were listed in **Table 2.2**. A study was excluded if it is based on a subpopulation of an included study. Reviews, conference abstracts, letters, case reports, and editorials were also excluded. We extracted the information of first author, year of publication, name of the study, country where the study was conducted, study type, study period, age range of participants, percentage male, indicators measurement, and number of participants. When relevant data were unclear in the paper, we directly contacted authors of the study for more details. Two investigators (YP and SC) independently assessed the articles and extracted information, and disagreements were resolved by consensus.

Table 2.1 Searching details of the meta-analysis.

Database	Search strategy
PubMed	# 1 (((("cardiovascular health") OR "CVH") OR "Life's Simple 7") OR "Life Simple 7") OR "LS7" # 2 (("American Heart Association"[MeSH Terms]) OR "American Heart Association") OR "AHA" # 3 ("adult"[MeSH Terms]) OR "adult" #4 #1 AND #2 AND #3
Embase	# 1 'cardiovascular health'/exp OR 'cardiovascular health' OR 'CVH' OR 'life* simple 7' OR 'life simple 7' OR 'LS7' # 2 'american heart association' OR 'aha' # 3 'adult'/exp OR 'adult' # 4 #1 AND #2 AND #3
Cochrane Central Register of Controlled Trials	#1 "cardiovascular health" OR "CVH" OR "Life's Simple 7" OR "Life Simple 7" OR "LS7" #2 MeSH descriptor: [American Heart Association] explode all trees OR "American Heart Association" OR "AHA" #3 MeSH descriptor: [Adult] explode all trees OR "adult" #4 #1 AND #2 AND #3

Table 2.2 Definitions of AHA's ideal CVH metrics.

Metrics	Definitions
Smoking	Never or quit > 12 months
BMI	< 25 kg/m^2
Physical activity	≥ 150 min/week moderate intensity or ≥ 75 min/week vigorous intensity or ≥ 150 min/week moderate + vigorous
Dietary pattern	4-5 components of the following: 1) Fruits and vegetables: ≥ 4.5 cups per day 2) Fishes: ≥ two 3.5-oz servings per week 3) Fiber-rich whole grains (≥ 1.1 g of fiber per 10 g of carbohydrate): ≥ three 1-oz-equivalent servings per day 4) Sodium: < 1500 mg per day 5) Sugar-sweetened beverages: ≤ 450 kcal (36 oz) per week
TC	< 200 mg/dL, untreated
BP	< 120/80 mm Hg, untreated
FPG	< 100 mg/dL, untreated

Abbreviations: AHA, American Heart Association; CVH, cardiovascular health; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

Study risk of bias

We assessed the quality of included studies using the risk of bias tool for prevalence studies, which was developed by Hoy and colleagues. [24] It consisted of 10 items and response options for each item was either yes or no. Studies with yes answered for 0 to 3, 4 to 6, and 7 to 10 items were regarded as having overall high, moderate and low risk of bias, respectively. Two investigators (YP and SC) evaluated the risk of bias separately, with disagreements reconciled through discussion.

Statistical analysis

We calculated the pooled prevalence of ideal status and the corresponding 95% confidence intervals (CIs) for each of the seven CVH metrics. In addition, we calculated the pooled prevalence and 95% CIs for overall poor and ideal CVH. We used I^2 statistic to quantify the heterogeneity between studies. A random-effect model was utilized if $I^2 > 30\%$, as it indicated possible moderate or high heterogeneity. Otherwise, a fixed-effect model was applied. We carried out subgroup analyses stratified by sex, age, region, and study period to investigate potential sources of heterogeneity. Subjects were classified into young (< 60 years) and older (≥ 60) age groups. Studies were stratified into six regions based on the continents they were conducted: North America, Asia, Europe, South America, Oceania, and Africa. We divided the study period into 1983-2000, 2001-2010, and 2011-2018 and the study period of an included study was determined by its median study year. Firstly, we performed the overall and subgroup analyses based on all the eligible studies (model 1). Then, we excluded the studies that modified the AHA's definitions of ideal CVH metrics to remove the potential influences of misclassifications (model 2). As both objective measurements and self-reported questionnaires were used for BMI, physical activity, TC, BP, and FPG, we compared the prevalence by scales for the five metrics. We used Begg's rank correlation method to measure the publication bias, with a significant level of $P < 0.1$. [25] To evaluate the influence of any possible publication bias, we used the trim and fill method by adding potentially missing studies for the analyses with significant Begg's test results. We did all the data analyses using the Stata software, version 14.1 (StataCorp, College Station, Texas, USA).

Results

Literature flow

We identified 1112 articles from the literature search and 21 through reference lists search. After the title, abstract and full-text review, 88 studies were finally included in our study [26-113] (**Figure 2.1**) and the full list and general characteristics of the included studies were available in **Table 2.3**. Due to the significant heterogeneity (I^2>95%), we applied a random-effect model for all the analyses. We divided the study of Yang Q *et al* [30] into two studies, conducted in 1988-1994 and 1999-2010, respectively, for assessing the study period differences. Similarly, we analysed the US and Luxembourg subjects separately when stratified by continents for another study. [45]

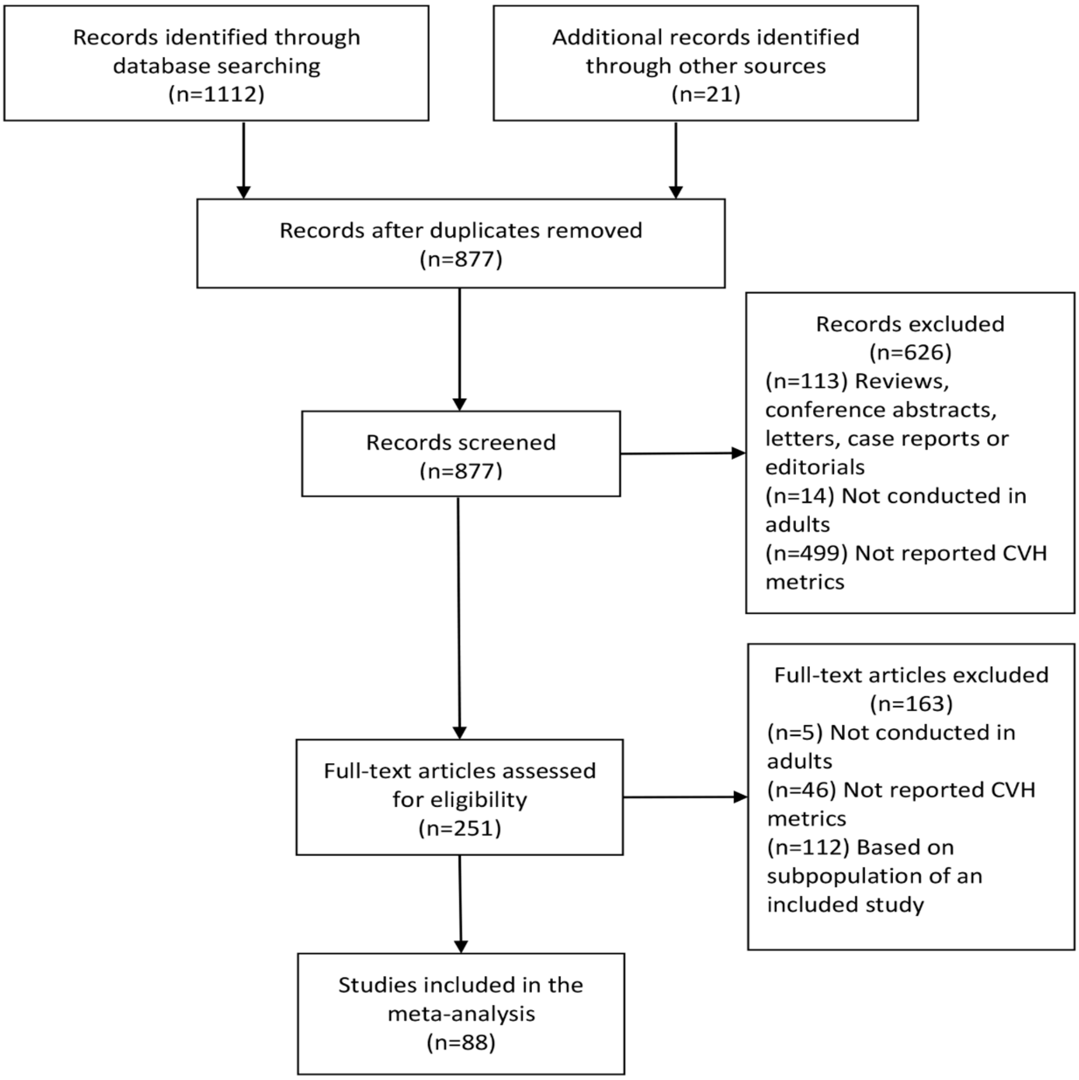


Figure 2.1 Flow chart of studies selection.

Table 2.3 General characteristics of the included studies.

Ref.	First author, publication year	Name of study	Location	Study type	Study period	Total participants	Age range (years)	% Male	Indicators measurement
26	Bambs C, 2011	Heart SCORE	US	CS	2003	1933	45-75	34	Individual
27	Artero EG, 2012	ACLS	US	Cohort	1987-1999	11993	20-88	76	Individual Combined
28	Fang J, 2012	BRFSS	US	CS	2009	356441	≥ 18	37	Combined
29	Wu S, 2012	Kailuan Cohort	China	Cohort	2006-2007	91698	18-98	79	Individual
30	Yang Q, 2012	NHANES	US	Cohort	1988-1994 1999-2010	44959	≥ 20	49	Individual Combined
31	Del Brutto OH, 2013	The Atahualpa Project	Ecuador	CS	2012	616	≥ 40	41	Individual Combined
32	Forget G, 2013	NA	Canada	Cohort	2006-2007	196	≥ 18	27	Individual Combined
33	Graciani A, 2013	Study on Nutrition and Cardiovascular Risk	Spain	CS	2008-2010	11408	≥ 18	49	Individual Combined
34	Kim JI, 2013	HONU	US	CS	2009, 2011	4754	≥ 18	42	Individual Combined
35	Kim JY, 2013	Seoul Male Cohort Study	South Korea	Cohort	1993	14533	40-59	100	Individual Combined
36	Kulshreshtha A, 2013	REGARDS	US	Cohort	2003-2007	22914	≥ 45	42	Combined

37	Lee HJ, 2013	KNHANES	South Korea	CS	2005,2007-2009	18059	≥ 20	41	Individual Combined
38	Rasmussen-Torvik LJ, 2013	ARIC	US	Cohort	1987-1989	13253	45-64	45	Combined
39	Reis JP, 2013	CARDIA	US	Cohort	2010-2011	2932	43-55	45	Individual Combined
40	Wu HY, 2013	CHED	China	CS	2009-2010	1012418	20-65	54	Individual
41	Zeng Q, 2013	DREHM	China	CS	2009-2012	9962	20-83	56	Individual Combined
42	Zhang Q, 2013	Kailuan Cohort	China	Cohort	2006-2007	91698	18-98	79	Combined
43	Aatola H, 2014	The Cardiovascular Risk in Young Finns Study	US	CS	2007	1143	30-45	44	Individual
44	Alman AC, 2014	CACTI	US	Cohort	2000-2002	1177	20-55	47	Individual
45	Crichton GE, 2014	MSLS	US	CS	2001-2006	1818	30-69	46	Individual
		ORISCAV-LUX	Luxembourg		2007-2009				
46	Davis SK, 2014	RAHSS	US	CS	2004-2005	674	18-90	0	Individual
47	Felisbino-Mendes MS, 2014	NA	Brazil	CS	2008-2010	928	≥ 18	47	Individual
48	Fretts AM, 2014	SHFS	US	Cohort	2001-2003	1639	18-74	37	Individual
49	Jankovic S, 2014	2010 NHS in RS, Bosnia and Herzegovina	Republic of Srpska, Bosnia and Herzegovina	CS	2010	4170	≥ 18	46	Individual Combined

50	Kulshreshtha A, 2014	Emory Twin Study	US	CS	2002-2010	490	46-64	100	Individual
51	Moghaddam MM, 2014	TLGS	Iran	CS	2009-2011	4865	≥ 20	41	Individual Combined
52	Peltonen M, 2014	National FINRISK Study	Finland	CS	2007	4741	25-74	45	Individual Combined
53	Tully L, 2014	NA	US	CS	2010-2012	830	≥ 20	74	Individual Combined
54	Xanthakis V, 2014	Sixth cycle of Framingham Offspring Study	US	Cohort	1995-1998	2680	32-85	45	Combined
55	Bi Y, 2015	China Noncommunicable Disease Surveillance 2010	China	CS	2010	96121	≥ 20	46	Individual Combined
56	Cao X, 2015	CSWHSP	China	CS	2013-2014	1625	≥ 18	0	Individual Combined
57	Dhamoon MS, 2015	NOMAS	US	Cohort	1993-2001	3219	≥ 40	37	Individual Combined
58	Djoussé L, 2015	JHS	US	CS	2000-2013	5301	≥ 20	37	Individual Combined
59	Laitinen TT, 2015	The Cardiovascular Risk in Young Finns Study	Finland	CS	2007	1465	33-45	44	Combined
60	Loucks EB, 2015	LEAP	US	CS	2010-2011	382	36-52	43	Individual Combined
61	O'Flynn AM, 2015	Mitchelstown study	Ireland	CS	2010-2011	362	50-69	49	Individual

62	Ogunmoroti O, 2015	BHSF	US	CS	2014	9364	18-85	26	Individual Combined
63	Olson NC, 2015	REGARDS	US	Cohort	2003-2007	27028	≥ 45	45	Individual
64	Robbins JM, 2015	NHLBI FHS	US	Cohort	1993-1995	1731	45-69	41	Individual Combined
65	Sturlaugsdottir R, 2015	AGES-Reykjavik	Iceland	CS	2002-2006	219	67-99	34	Individual Combined
66	Velasquez-Melendez G, 2015	PNS	Brazil	CS	2013	34362	≥ 18	49	Individual
67	Chang Y, 2016	NCRCHS	China	CS	2012-2013	11113	≥ 35	46	Individual Combined
68	Chou LP, 2016	NA	China	CS	2012	1329	21-64	17	Individual Combined
69	Foraker RE, 2016	WHI	US	Cohort	2010	145385	50-79	0	Combined
70	Gaye B, 2016	PPS III	France	CS	2008-2012	9417	50-75	61	Combined
71	Gibbs BB, 2016	IDEA	US	CS	2010-2012	335	18-35	32	Individual Combined
72	González HM, 2016	HCHS/SOL	US	CS	2008-2011	15825	18-74	43	Individual Combined
73	Graciani A, 2016	NA	Spain	Cohort	2008-2010	1745	≥ 60	49	Individual Combined
74	Luo TY, 2016	NA	China	CS	2013-2014	2795	≥ 40	50	Individual Combined
75	Ogunmoroti O, 2016	BHSF	US	CS	2011-2013	25382	18-85	25	Individual Combined

76	Pase MP, 2016	Seventh cycle of Framingham Offspring Study	US	Cohort	1998-2001	2631	≥ 45	45	Combined
77	Ren J, 2016	SMASH	China	CS	2011-2015	15350	18-69	50	Individual Combined
78	Saiz AM, 2016	SHOW	US	CS	2008-2014	2935	21-74	50	Individual
79	Shen S, 2016	NA	China	CS	2014-2015	27824	40-64	100	Individual
80	Zhao Y, 2016	NA	China	CS	2010	2693	20-80	33	Individual
81	Benderly M, 2017	Hadera District Study	Israel	CS	2002-2007	1104	25-74	50	Individual Combined
82	Feinstein MJ, 2017	UGANDAC	Uganda	CS	2005	205	> 40	49	Individual Combined
83	Fernandez-Alvira JM, 2017	PESA	Spain	CS	2010-2013	3983	40-54	63	Individual Combined
84	Gaye B, 2017	Three-City Study	France	Cohort	1999-2001	7371	≥ 65	37	Individual Combined
85	Gaye B, 2017	PRIME	Northern Ireland, France	Cohort	1991-1993	9312	50-59	100	Combined
86	Gupta B, 2017	NA	India	CS	2006-2010	6198	20-75	55	Individual Combined
87	Jin Y, 2017	InCHIANTI	Italy	Cohort	1998-2000	928	≥ 65	45	Individual
88	Lawrence E, 2017	Add Health IV	US	CS	2008-2009	12253	24-34	47	Individual
89	Manczuk M, 2017	PONS	Poland	CS	2010-2011	10687	45-64	34	Individual
90	Matthews KA, 2017	PYS	US	Cohort	2007	307	30-41	100	Individual

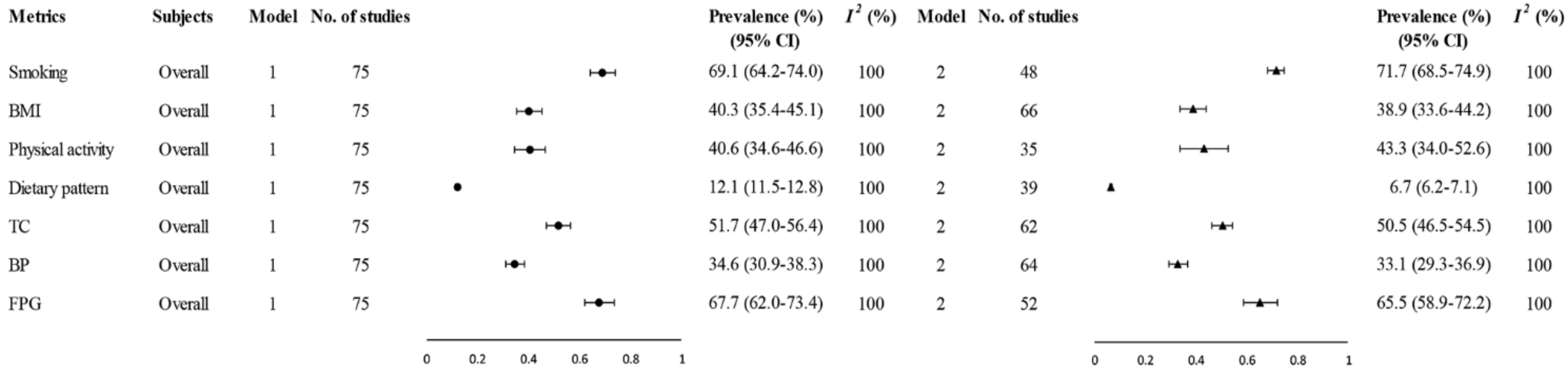
91	Ogunmoroti O, 2017	MESA	US	Cohort	2000-2002	6506	45-84	47	Individual Combined
92	Perrot N, 2017	EPIC-Norfolk	UK	Cohort	1993-1997	14051	39-79	47	Individual
93	Shen S, 2017	NA	China	CS	2014-2015	26701	40-64	100	Combined
94	Simon M, 2017	PPS III	France	CS	2008-2012	9012	50-75	61	Individual
95	Slopen N, 2017	MIDUSII	US	CS	2004-2005	1147	34-84	44	Individual
96	Talegawkar SA, 2017	MASALA	US	CS	2010-2013	875	40-84	53	Individual Combined
97	Veromaa V, 2017	PORi To Aid Against Threats	Finland	CS	2014	732	19-66	0	Combined
98	Wang Y, 2017	COACS	China	CS	2013-2014	4313	18-64	40	Individual
99	Wang YQ, 2017	NA	China	CS	2014-2016	3009	≥ 20	67	Individual Combined
100	Windham BG, 2017	ARIC	US	Cohort	1987-1989	15744	45-64	45	Individual
101	Benziger CP, 2018	CRONICAS	Peru	CS	2010	3058	≥ 35	49	Individual Combined
102	Bueno-Antequera J, 2018	NA	Spain	CS	2014-2017	142	18-61	76	Individual
103	García-Hermoso A, 2018	Chilean National Health Survey	Chile	CS	2009-2010	460	> 65	41	Individual Combined
104	García-Hermoso A, 2018	EVIDENT	Spain	CS	2006	1365	20-80	40	Individual Combined
105	Han C, 2018	China-PAR	China	Cohort	1998 2000-2001 2007-2008	93987	≥ 20	40	Individual Combined
106	Landi F, 2018	Lookup 7+	Italy	CS	2015-2017	6323	≥ 18	43	Individual Combined

107	Machado LBM, 2018	ELSA-Brasil	Brazil	CS	2008-2010	13356	35-74	45	Individual
108	Nguyen XT, 2018	MVP	US	CS	2011-2017	201745	≥ 18	92	Individual Combined
109	Peng Y, 2018	AHS	Australia	CS	2011-2012	7499	≥ 18	44	Individual Combined
110	Seron P, 2018	CESCAS I	Argentina Chile Uruguay	CS	2011-2012	7524	35-74	41	Individual Combined
111	Sjöholm P, 2018	ABC	Australia	CS	2014-2016	467	24-29	47	Individual
112	Szlejf C, 2018	ELSA-Brasil	Brazil	CS	2008-2010	13743	35-74	45	Combined
113	Zhou L, 2018	PRC-USA	China	Cohort	1983-1984	938	35-59	50	Individual Combined

Abbreviations: SCORE, Strategies Concentrating on Risk Evaluation; CS, cross-sectional; ACLS, Aerobics Center Longitudinal Study; BRFSS, Behavioral Risk Factor Surveillance System; NHANES, National Health and Nutrition Examination Survey; NA, not available; HONU, Heart of New Ulm; REGARDS, Reasons for Geographic and Racial Differences in Stroke; KNHANES, Korean National Health and Nutrition Examination Survey; ARIC, Atherosclerosis Risk In Communities; CARDIA, Coronary Artery Risk Development in Young Adults; CHED, Chinese Health Examination Database; DREHM, Disease Risk Evaluation and Health Management; CACTI, Coronary Artery Calcification in Type 1 Diabetes; MSLS, Maine-Syracuse Longitudinal Study; ORISCAV-LUX, Observation of Cardiovascular Risk Factors in Luxembourg; RAHSS, Regional Assessment Health Surveillance Study; SHFS, Strong Heart Family Study; TLGS, Tehran Lipid and Glucose Study; CSWHSP, Changsha Women's Health Screening Program; NOMAS, Northern Manhattan Study; JHS, Jackson Heart Study; LEAP, Longitudinal Effects on Aging Perinatal; BHSF, Baptist Health South Florida; NHLBI FHS, National Heart, Lung, and Blood Institute Family Heart Study; AGES, Age, Gene/ Environment Susceptibility; PNS, Population National health Survey; NCRCHS, Northeast China Rural Cardiovascular Health Study; WHI, Women's Health Initiative; PPS, Paris Prospective Study; IDEA, Innovative approaches to Diet, Exercise, and Activity; HCHS/SOL, Hispanic Community Health Study / Study of Latinos; SMASH, Shandong province and the Chinese Ministry of Health collaborative Action on Salt reduction and Hypertension; SHOW, Survey of the Health of Wisconsin; UGANDAC, Ugandan Non-communicable Diseases and Aging Cohort; PESA, Progression of Early Subclinical Atherosclerosis; PRIME, Prospective Epidemiological Study of Myocardial Infarction; PONS, Polish Norwegian Study; PYS, Pittsburgh Youth Study; MESA, Multi-Ethnic Study of Atherosclerosis; EPIC, European Prospective Investigation into Cancer and Nutrition; MIDUS, Midlife in the United States; MASALA, Mediators of Atherosclerosis in South Asians Living in America; COACS, China Suboptimal Health Cohort Study; PAR, Prediction for ASCVD Risk; MVP, Million Veteran Program; AHS, Australian Health Survey; CESCAS, Detection and follow-up of cardiovascular disease and risk factors in the Southern Cone of Latin America; ABC, Aboriginal Birth Cohort.

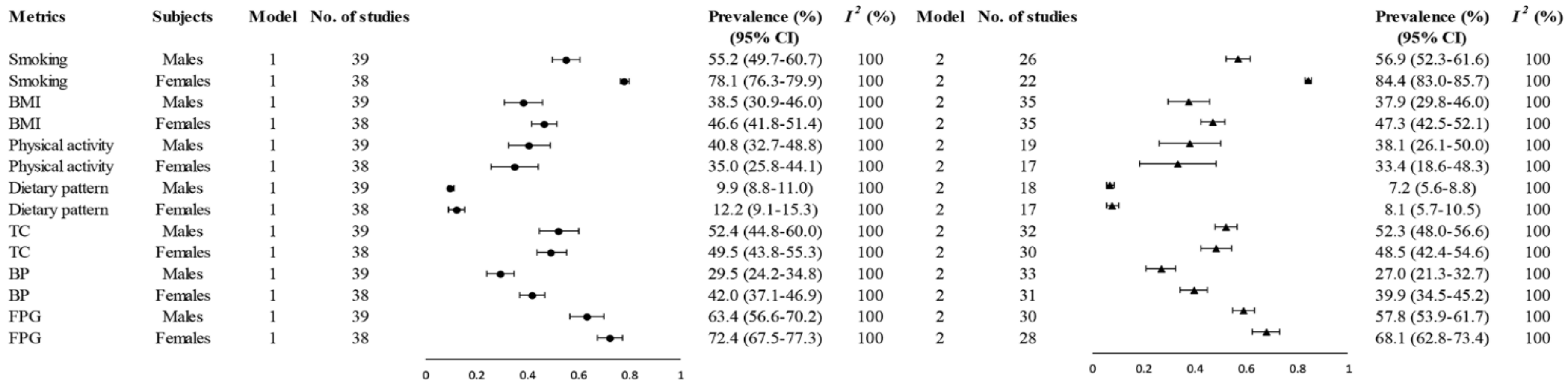
Prevalence of ideal CVH metrics

There were 75 studies reported the prevalence of ideal CVH metrics. [26, 27, 29-35, 37, 39-41, 43-53, 55-58, 60-68, 71-75, 77-84, 86-92, 94-96, 98-111, 113] Smoking had the highest prevalence of ideal status (69.1%; 95% CI: 64.2% to 74.0%), followed by FPG (67.7%; 95% CI: 62.0% to 73.4%), TC (51.7%; 95% CI: 47.0% to 56.4%), physical activity (40.6%; 95% CI: 34.6% to 46.6%), BMI (40.3%; 95% CI: 35.4% to 45.1%), BP (34.6%; 95% CI: 30.9% to 38.3%), and dietary pattern (12.1%; 95% CI: 11.5% to 12.8%) (model 1) and the ranking did not change after restricted to those followed AHA's guideline (**Figure 2.2**). We observed that, from both models, males had greater proportions of ideal TC and physical activity, whereas females had higher estimates of ideal status for the other five metrics (**Figure 2.3**). Older subjects were more likely to have ideal status for smoking and dietary pattern and less likely to have optimal status for other metrics than did young adults (**Figure 2.4**). Since most studies were conducted in North America, Asia and Europe (88%, 66/75), we made proportion comparisons between the three regions. Results from both models indicated that Asians had the highest ideal percentages in BMI, TC, and BP, whereas North Americans and Europeans had the greatest frequencies in smoking and dietary pattern, respectively. For ideal physical activity, North Americans ranked the first in ideal proportion when analysed all the participants, while Europeans ranked the first after excluded those did not follow the AHA's definition. Europeans, in model 1, had the greatest frequency in ideal FPG. However, North Americans had the greatest ideal FPG frequency in model 2 (**Figure 2.5**). We observed the monotonous raising tendency with study period regarding the proportions of ideal physical activity, TC, and BP in both models. The proportions of ideal FPG, in both models, displayed a dropped trend from 1983 to 2010 and experienced elevation since 2011. For the proportion of ideal smoking, the findings of model 1 revealed an increasing trend over time while it altered to a U-shaped in model 2. The ideal BMI prevalence displayed a U-shaped relationship in model 1 and it changed to a reversed U-shape in model 2. The secular trend was a U-shaped for the prevalence of ideal dietary pattern in all the eligible studies, but it shifted to an increasing pattern when restricted to the studies that followed the AHA's definition (**Figure 2.6**). The different scales had little effect on the prevalence of ideal metrics (data not shown).



Metrics	Subjects	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)
Smoking	Overall	1	75	69.1 (64.2-74.0)	100	2	48	71.7 (68.5-74.9)	100
BMI	Overall	1	75	40.3 (35.4-45.1)	100	2	66	38.9 (33.6-44.2)	100
Physical activity	Overall	1	75	40.6 (34.6-46.6)	100	2	35	43.3 (34.0-52.6)	100
Dietary pattern	Overall	1	75	12.1 (11.5-12.8)	100	2	39	6.7 (6.2-7.1)	100
TC	Overall	1	75	51.7 (47.0-56.4)	100	2	62	50.5 (46.5-54.5)	100
BP	Overall	1	75	34.6 (30.9-38.3)	100	2	64	33.1 (29.3-36.9)	100
FPG	Overall	1	75	67.7 (62.0-73.4)	100	2	52	65.5 (58.9-72.2)	100

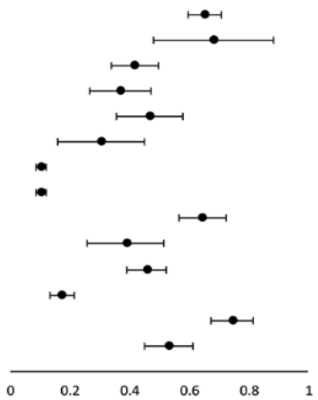
Figure 2.2 Pooled proportions of the ideal CVH metrics in the overall population. Abbreviations: BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CI, confidence interval; CVH, cardiovascular health.



Metrics	Subjects	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)
Smoking	Males	1	39	55.2 (49.7-60.7)	100	2	26	56.9 (52.3-61.6)	100
Smoking	Females	1	38	78.1 (76.3-79.9)	100	2	22	84.4 (83.0-85.7)	100
BMI	Males	1	39	38.5 (30.9-46.0)	100	2	35	37.9 (29.8-46.0)	100
BMI	Females	1	38	46.6 (41.8-51.4)	100	2	35	47.3 (42.5-52.1)	100
Physical activity	Males	1	39	40.8 (32.7-48.8)	100	2	19	38.1 (26.1-50.0)	100
Physical activity	Females	1	38	35.0 (25.8-44.1)	100	2	17	33.4 (18.6-48.3)	100
Dietary pattern	Males	1	39	9.9 (8.8-11.0)	100	2	18	7.2 (5.6-8.8)	100
Dietary pattern	Females	1	38	12.2 (9.1-15.3)	100	2	17	8.1 (5.7-10.5)	100
TC	Males	1	39	52.4 (44.8-60.0)	100	2	32	52.3 (48.0-56.6)	100
TC	Females	1	38	49.5 (43.8-55.3)	100	2	30	48.5 (42.4-54.6)	100
BP	Males	1	39	29.5 (24.2-34.8)	100	2	33	27.0 (21.3-32.7)	100
BP	Females	1	38	42.0 (37.1-46.9)	100	2	31	39.9 (34.5-45.2)	100
FPG	Males	1	39	63.4 (56.6-70.2)	100	2	30	57.8 (53.9-61.7)	100
FPG	Females	1	38	72.4 (67.5-77.3)	100	2	28	68.1 (62.8-73.4)	100

Figure 2.3 Pooled proportions of the ideal CVH metrics in males and females. Abbreviations: BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CI, confidence interval; CVH, cardiovascular health.

Metrics	Subjects	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)
Smoking	Young	1	23	65.1 (59.6-70.6)	100	2	15	66.6 (59.6-73.6)	100
Smoking	Older	1	17	68.0 (47.8-88.1)	100	2	11	71.9 (61.8-82.0)	100
BMI	Young	1	23	41.6 (33.7-49.6)	100	2	19	39.2 (29.8-48.5)	100
BMI	Older	1	17	36.9 (26.8-47.1)	100	2	16	36.8 (26.2-47.3)	100
Physical activity	Young	1	23	46.7 (35.5-58.0)	100	2	10	44.1 (26.1-62.2)	100
Physical activity	Older	1	17	30.6 (16.1-45.1)	100	2	6	37.0 (8.7-65.2)	100
Dietary pattern	Young	1	23	10.4 (8.7-12.0)	100	2	10	10.3 (8.1-12.5)	100
Dietary pattern	Older	1	17	10.2 (8.5-12.0)	99	2	7	12.9 (6.1-19.7)	100
TC	Young	1	23	64.4 (56.4-72.4)	100	2	17	62.1 (52.4-71.8)	100
TC	Older	1	17	38.8 (25.9-51.6)	100	2	15	37.8 (22.2-53.4)	100
BP	Young	1	23	45.7 (39.1-52.2)	100	2	19	42.7 (37.2-48.3)	100
BP	Older	1	17	17.2 (13.2-21.3)	100	2	13	13.1 (9.4-16.7)	99
FPG	Young	1	23	74.5 (67.3-81.6)	100	2	15	71.7 (64.8-78.5)	100
FPG	Older	1	17	53.2 (45.2-61.2)	100	2	14	50.8 (41.2-60.3)	100



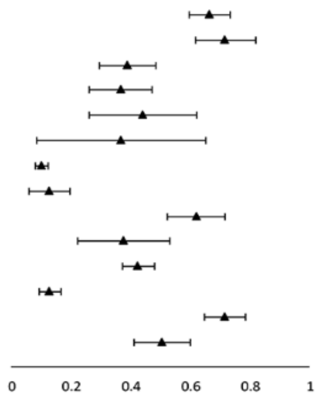
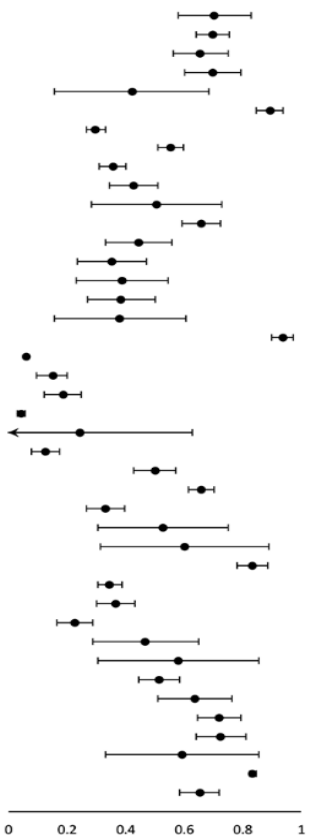
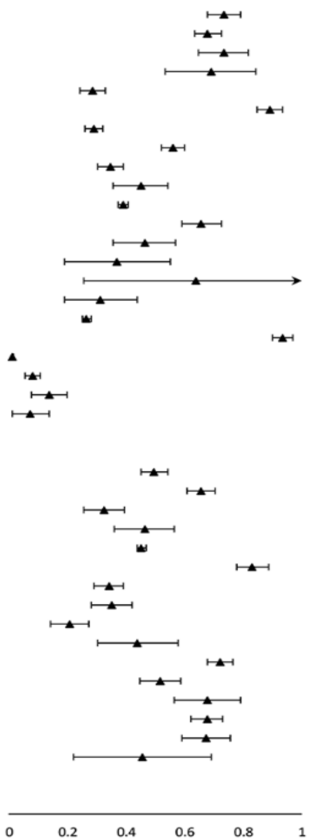


Figure 2.4 Pooled proportions of the ideal CVH metrics in young and older adults. Abbreviations: BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CI, confidence interval; CVH, cardiovascular health.

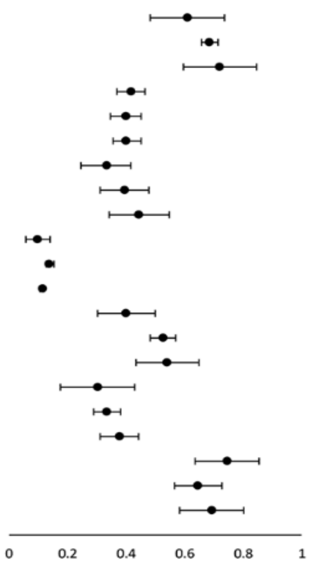




Metrics	Subjects	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)
Smoking	North America	1	30	70.5 (57.9-83.0)	100	2	19	73.8 (68.1-79.4)	100
Smoking	Asia	1	20	69.7 (64.0-75.4)	100	2	14	68.0 (63.4-72.6)	100
Smoking	Europe	1	16	65.6 (56.3-75.0)	100	2	9	73.4 (64.7-82.0)	100
Smoking	South America	1	7	69.7 (60.1-79.3)	100	2	5	69.1 (53.7-84.4)	100
Smoking	Oceania	1	2	42.2 (15.9-68.6)	99	2	1	28.7 (24.2-33.2)	NA
Smoking	Africa	1	1	89.3 (84.8-93.8)	NA	2	1	89.3 (84.8-93.8)	NA
BMI	North America	1	30	29.9 (26.7-33.1)	100	2	29	29.3 (26.3-32.3)	100
BMI	Asia	1	20	55.5 (51.2-59.7)	100	2	15	56.1 (52.1-60.1)	100
BMI	Europe	1	16	35.8 (31.3-40.4)	99	2	15	34.8 (30.3-39.4)	99
BMI	South America	1	7	42.9 (34.6-51.1)	100	2	6	45.3 (35.9-54.6)	100
BMI	Oceania	1	2	50.5 (28.2-72.8)	99	2	1	39.2 (37.3-41.1)	NA
BMI	Africa	1	1	65.9 (59.2-72.6)	NA	2	1	65.9 (59.2-72.6)	NA
Physical activity	North America	1	30	44.6 (33.3-55.9)	100	2	15	46.4 (35.8-56.9)	100
Physical activity	Asia	1	20	35.3 (23.6-47.0)	100	2	11	37.2 (19.2-55.2)	100
Physical activity	Europe	1	16	38.8 (23.1-54.4)	100	2	3	64.1 (25.5-102.8)	100
Physical activity	South America	1	7	38.6 (27.1-50.1)	100	2	5	31.4 (19.1-43.8)	100
Physical activity	Oceania	1	2	38.1 (15.5-60.6)	99	2	1	26.7 (25.2-28.2)	NA
Physical activity	Africa	1	1	93.7 (90.1-97.3)	NA	2	1	93.7 (90.1-97.3)	NA
Dietary pattern	North America	1	30	6.0 (5.7-6.3)	100	2	18	1.5 (1.3-1.6)	99
Dietary pattern	Asia	1	20	15.1 (9.9-20.4)	100	2	11	8.1 (5.5-10.8)	100
Dietary pattern	Europe	1	16	18.6 (12.3-24.9)	100	2	7	14.0 (7.8-20.2)	100
Dietary pattern	South America	1	7	4.3 (2.9-5.6)	99	2	3	7.6 (1.1-14.1)	98
Dietary pattern	Oceania	1	2	24.3 (-14.2-62.8)	99	2	0	NA	NA
Dietary pattern	Africa	1	1	12.7 (8.0-17.5)	NA	2	0	NA	NA
TC	North America	1	30	50.1 (43.0-57.2)	100	2	25	49.8 (45.3-54.3)	100
TC	Asia	1	20	65.8 (61.4-70.1)	100	2	17	65.7 (60.9-70.4)	100
TC	Europe	1	16	33.2 (26.6-39.8)	100	2	14	32.6 (25.6-39.6)	100
TC	South America	1	7	52.9 (30.6-75.3)	100	2	5	46.4 (36.3-56.5)	99
TC	Oceania	1	2	60.1 (31.3-88.9)	99	2	1	45.5 (43.8-47.2)	NA
TC	Africa	1	1	83.4 (78.1-88.7)	NA	2	1	83.4 (78.1-88.7)	NA
BP	North America	1	30	34.5 (30.3-38.6)	100	2	26	34.3 (29.4-39.1)	100
BP	Asia	1	20	36.7 (30.0-43.4)	100	2	18	35.1 (28.1-42.1)	100
BP	Europe	1	16	22.9 (16.8-29.0)	100	2	14	20.9 (14.4-27.3)	100
BP	South America	1	7	46.9 (28.9-64.9)	100	2	5	44.1 (30.4-57.8)	100
BP	Oceania	1	2	58.2 (30.6-85.7)	99	2	1	72.3 (68.0-76.6)	NA
BP	Africa	1	1	51.7 (44.7-58.8)	NA	2	1	51.7 (44.7-58.8)	NA
FPG	North America	1	30	63.6 (50.9-76.2)	100	2	20	67.9 (56.7-79.2)	100
FPG	Asia	1	20	72.0 (64.6-79.3)	100	2	17	67.8 (62.4-73.2)	100
FPG	Europe	1	16	72.7 (64.2-81.1)	100	2	11	67.4 (59.1-75.7)	100
FPG	South America	1	7	59.2 (32.9-85.4)	100	2	5	45.9 (22.4-69.3)	100
FPG	Oceania	1	2	83.5 (82.4-84.6)	0	2	0	NA	NA
FPG	Africa	1	1	65.4 (58.6-72.1)	NA	2	0	NA	NA

Figure 2.5 Pooled proportions of the ideal CVH metrics in six continents. Abbreviations: BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CI, confidence interval; NA, not available; CVH, cardiovascular health.

Metrics	Subjects	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)
Smoking	1983-2000	1	10	61.0 (48.2-73.8)	100	2	4	72.2 (50.6-93.9)	100
Smoking	2001-2010	1	38	68.6 (65.7-71.4)	100	2	24	70.6 (68.2-72.9)	100
Smoking	2011-2018	1	28	72.0 (59.5-84.6)	100	2	20	73.1 (63.8-82.5)	100
BMI	1983-2000	1	10	41.5 (36.7-46.3)	100	2	7	35.5 (30.8-40.3)	99
BMI	2001-2010	1	38	39.9 (34.5-45.4)	100	2	36	40.1 (34.5-45.7)	100
BMI	2011-2018	1	28	40.1 (35.4-45.0)	100	2	24	37.8 (30.6-45.1)	100
Physical activity	1983-2000	1	10	33.2 (24.5-41.9)	100	2	5	36.1 (33.5-38.6)	97
Physical activity	2001-2010	1	38	39.6 (31.3-47.9)	100	2	17	40.6 (26.2-55.1)	100
Physical activity	2011-2018	1	28	44.5 (34.2-54.9)	100	2	14	48.7 (32.3-65.2)	100
Dietary pattern	1983-2000	1	10	9.9 (5.8-13.9)	100	2	5	4.4 (1.0-7.7)	100
Dietary pattern	2001-2010	1	38	13.7 (12.0-15.4)	100	2	20	6.8 (5.6-8.0)	100
Dietary pattern	2011-2018	1	28	11.3 (10.6-11.9)	100	2	14	9.4 (8.1-10.7)	100
TC	1983-2000	1	10	40.1 (30.5-49.8)	100	2	7	33.2 (22.5-43.9)	100
TC	2001-2010	1	38	52.8 (48.4-57.1)	100	2	35	52.3 (47.7-56.9)	100
TC	2011-2018	1	28	54.1 (43.3-65.0)	100	2	21	53.0 (45.0-61.0)	100
BP	1983-2000	1	10	30.2 (17.4-42.9)	100	2	8	25.7 (14.4-36.9)	100
BP	2001-2010	1	38	33.5 (28.9-38.2)	100	2	35	32.8 (27.9-37.7)	100
BP	2011-2018	1	28	37.6 (31.2-44.1)	100	2	22	36.4 (29.8-43.1)	100
FPG	1983-2000	1	10	74.4 (63.5-85.4)	100	2	5	66.7 (51.6-81.8)	100
FPG	2001-2010	1	38	64.6 (56.4-72.7)	100	2	30	64.1 (54.8-73.3)	100
FPG	2011-2018	1	28	69.3 (58.5-80.1)	100	2	17	67.8 (61.9-73.7)	100



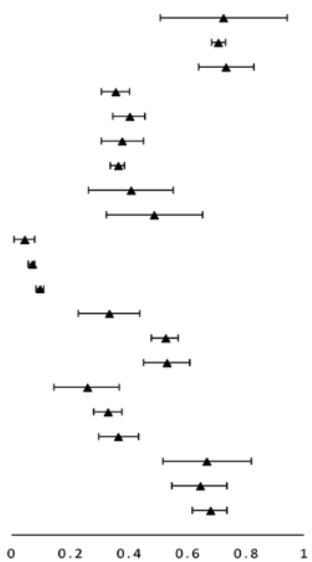
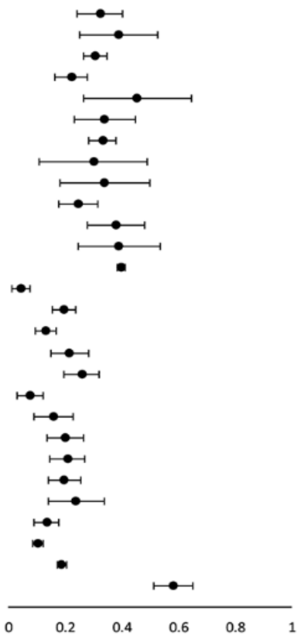


Figure 2.6 Pooled proportions of the ideal CVH metrics over study periods. Abbreviations: BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CI, confidence interval; CVH, cardiovascular health.

Prevalence of the overall poor and ideal CVH status

There were 58 [27, 28, 30-39, 41, 42, 49, 52-60, 62, 64, 65, 67-77, 81-86, 91, 93, 96, 97, 99, 101, 103-106, 108, 109, 112, 113] and 55 [27, 30-39, 41, 42, 49, 51-60, 62, 64, 65, 67-72, 74-77, 81-86, 93, 96, 97, 99, 101, 103-105, 108-110, 112] studies provided the proportions of overall poor and ideal CVH status, respectively. Our findings indicated that, in model 1, 32.2% (95% CI: 24.2% to 40.3%) and 19.6% (95% CI: 15.2% to 23.9%) participants were with poor and ideal CVH and the proportions were similar in model 2. Male participants were associated with a 28% higher rate of the poor CVH and a 39% lower rate of the ideal CVH when compared to those of females. Older adults displayed a more than doubled frequency of the poor CVH and a 71% lower proportion of the ideal CVH than did young adults. The sex and age disparities were generally consistent between the two models. Additionally, we compared the poor and ideal CVH status between North America, Asia, and Europe. For all the included studies, participants in Asia had the lowest poor CVH status and highest ideal CVH status. In contrast, adults from Europe had the highest poor CVH status and lowest ideal CVH status. Since only a few studies followed the AHA's definition, the ranking significantly altered in model 2. We also observed the declining proportion of poor CVH and rising proportion of ideal CVH over survey years and the findings were consistent between the two models (**Figure 2.7**).

CVH status	Subjects	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)	Model	No. of studies	Prevalence (%) (95% CI)	I^2 (%)
Poor	Oveall	1	58	32.2 (24.2-40.3)	100	2	15	31.0 (26.2-35.9)	100
Poor	Males	1	32	38.9 (25.0-52.8)	100	2	8	35.9 (26.8-44.9)	100
Poor	Females	1	32	30.5 (26.4-34.6)	100	2	9	25.1 (19.4-30.7)	100
Poor	Young	1	22	22.1 (16.5-27.7)	100	2	6	16.5 (12.5-20.5)	100
Poor	Older	1	20	45.5 (26.5-64.5)	100	2	5	33.9 (24.9-43.0)	100
Poor	1983-2000	1	11	34.0 (23.0-45.0)	100	2	2	48.0 (40.5-55.6)	98
Poor	2001-2010	1	27	33.2 (28.3-38.1)	100	2	6	30.0 (24.3-35.8)	100
Poor	2011-2018	1	21	29.9 (10.9-49.0)	100	2	7	26.9 (20.5-33.4)	100
Poor	North America	1	24	34.0 (18.2-49.8)	100	2	7	36.4 (22.5-50.4)	100
Poor	Asia	1	16	24.7 (17.9-31.5)	100	2	6	27.7 (19.4-35.9)	100
Poor	Europe	1	12	38.0 (27.9-48.2)	100	2	1	11.6 (10.6-12.6)	NA
Poor	South America	1	4	39.0 (24.4-53.6)	100	2	1	32.8 (29.0-36.6)	NA
Poor	Oceania	1	1	39.8 (38.4-41.2)	NA	2	0	NA	NA
Poor	Africa	1	1	4.4 (1.3-7.5)	NA	2	0	NA	NA
Ideal	Oveall	1	55	19.6 (15.2-23.9)	100	2	15	19.6 (14.8-24.5)	100
Ideal	Males	1	32	13.2 (9.4-16.9)	100	2	10	14.2 (10.1-18.3)	100
Ideal	Females	1	32	21.6 (15.1-28.1)	100	2	11	28.3 (20.8-35.8)	100
Ideal	Young	1	21	25.8 (19.5-32.1)	100	2	7	31.3 (24.8-37.8)	100
Ideal	Older	1	19	7.5 (2.9-12.0)	100	2	6	11.0 (3.8-18.2)	100
Ideal	1983-2000	1	10	15.9 (9.0-22.8)	100	2	2	8.0 (1.0-14.9)	100
Ideal	2001-2010	1	25	20.1 (13.6-26.6)	100	2	6	18.6 (11.2-26.0)	100
Ideal	2011-2018	1	21	20.8 (14.5-27.1)	100	2	7	23.8 (17.5-30.2)	99
Ideal	North America	1	22	19.6 (13.9-25.4)	100	2	6	14.5 (6.1-22.9)	100
Ideal	Asia	1	16	23.9 (14.2-33.6)	100	2	7	21.7 (15.7-27.8)	100
Ideal	Europe	1	10	13.4 (9.0-17.7)	100	2	1	42.1 (40.5-43.7)	NA
Ideal	South America	1	5	10.2 (8.3-12.0)	94	2	1	13.0 (10.2-15.7)	NA
Ideal	Oceania	1	1	18.7 (17.1-20.3)	NA	2	0	NA	NA
Ideal	Africa	1	1	58.6 (51.1-65.0)	NA	2	0	NA	NA



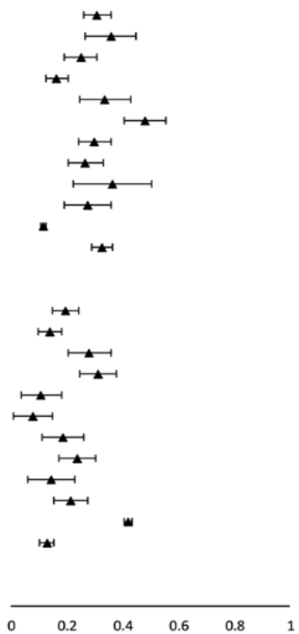


Figure 2.7 Pooled proportions of the overall poor and ideal CVH status. Abbreviations: CVH, cardiovascular health; CI, confidence interval; NA, not available.

Study quality and publication bias

Of the 88 included studies, 8 (9%) were regarded as having a moderate risk of bias and the others were having a low risk of bias (**Table 2.4**). There was no indication of significant publication bias for proportions of ideal smoking, physical activity, TC, BP, and FPG ($P > 0.1$ for Begg's test). There was potential significant publication bias for proportions of ideal BMI, dietary pattern, as well as the percentages of the overall poor and ideal CVH ($P < 0.1$ for Begg's test). Nevertheless, the results altered slightly after included the missing studies identified through the trim and fill method (data not shown).

Table 2.4 Quality assessment of the included studies.

Ref.	Item 1*	Item 2*	Item 3*	Item 4*	Item 5*	Item 6*	Item 7*	Item 8*	Item 9*	Item 10*	Overall risk of bias
26	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
27	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
28	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
29	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
30	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
31	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
32	No	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
33	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
34	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
35	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
36	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
37	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
38	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
39	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
40	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
41	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
42	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
43	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
44	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
45	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
46	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
47	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
48	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
49	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
50	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
51	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
52	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
53	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
54	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
55	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
56	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
57	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

58	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
59	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
60	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
61	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
62	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
63	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
64	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
65	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
66	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
67	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
68	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
69	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
70	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
71	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
72	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
73	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
74	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
75	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
76	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
77	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
78	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
79	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
80	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
81	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
82	No	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
83	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
84	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
85	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
86	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
87	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
88	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
89	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
90	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
91	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

92	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
93	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
94	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
95	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
96	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
97	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
98	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
99	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
100	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
101	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
102	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
103	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
104	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
105	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
106	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
107	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
108	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Moderate risk
109	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low risk
110	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
111	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
112	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk
113	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Low risk

* Item 1: Was the study's target population a close representation of the national population in relation to relevant variables?
Item 2: Was the sampling frame a true or close representation of the target population?
Item 3: Was some form of random selection used to select the sample, OR, was a census undertaken?
Item 4: Was the likelihood of non-response bias minimal?
Item 5: Were data collected directly from the subjects?
Item 6: Was an acceptable case definition used in the study?
Item 7: Was the study instrument that measured the parameter of interest shown to have reliability and validity?
Item 8: Was the same mode of data collection used for all subjects?
Item 9: Was the length of the shortest prevalence period for the parameter of interest appropriate?
Item 10: Were the numerator and denominator for the parameter of interest appropriate?

Discussion

This study observed that ideal status was most prevalent for smoking and was least prevalent for dietary pattern. Nearly one-third of participants were with the overall poor CVH status, while, in contrast, only less than one-fifth were with the overall ideal CVH status. Females and young adults had higher frequencies of ideal status for most metrics and better overall CVH status than their males and older counterparts. We also observed the disparities in the proportions of ideal CVH metrics and overall CVH status across continents. In addition, our findings indicated the improvement over survey periods in most CVH metrics and overall CVH status.

We have identified smoking and FPG as two metrics with the highest ideal levels and the finding was in agreement with the findings of a previous systematic review. [11] They observed that 21 out of 29 studies had ideal smoking and FPG percentages greater than 60%. The high optimal prevalence of smoking status may partly be explained by the effectiveness of governmental tobacco control policies, including mass media campaigns and the rise of tobacco products' price. [114, 115] The appealing ideal FPG proportion may partially due to the subtle improvement of physical activity [116, 117] and dietary pattern, [118] which were found to be significant influencing factors of diabetes and elevated FPG. [119] In contrast, our study revealed that merely 12.1% and 34.6% of participants were having ideal dietary pattern and BP and the proportions even dropped when we applied strict AHA definitions, which was in agreement with the previous systematic review. [11] The poor status of dietary pattern was also noticed in several large-scale studies. In a Chinese cohort with around 0.5 million adults, only 7% of participants were classified as having an ideal status of dietary pattern. [5] An Australian nationally representative survey indicated that 72% of adults did not meet the recommended amount of whole grain intake. [120] Our results of BP status were generally in line with two recent reports from two nationally representative surveys from US and China. [16, 121] They reported that merely 42.3% and 35.5% of US and Chinese adults reached BP level below 120/80 mm Hg. To be noticed, the American College of Cardiology/AHA released a guideline in 2017 and lowered the thresholds of defining hypertension, [122] which in turn greatly raised the prevalence and hypertension-related CVD burden. [123] Thus, our findings underscored the importance of dietary pattern and BP promotion in improving the overall CVH status and reducing the related CVD burden. We reported that 51.7%, 40.6% and 40.3% of participants were having ideal TC, physical activity, and BMI. Compared to the recent US nationally statistics indicated by AHA's 2018 update, [21] we reported a higher proportion of ideal BMI and lower proportions of ideal TC and physical activity. Since our results were collected from a global scale during 1983-2018, the decreasing trend in ideal BMI and increasing trend in ideal TC and physical activity, along with the possible regional disparities in metrics distribution, could partially account for the variations. [117, 124, 125]

Although applied a less strict definition of the overall ideal CVH (five to seven ideal metrics) [70] when compared to the definition of AHA (seven ideal metrics), [7] we noted that less than twenty percent of participants were with the overall ideal CVH status. In contrast, more than thirty percent of subjects were deemed as having a poor CVH status. Our findings were in agreement with a previous systematic review by Younus A *et al.* [11] They reported that, according to our ideal and poor CVH definitions, 17 out of 25 studies reported a poor CVH status proportion greater than 30% and 16 out of 25 studies reported an ideal CVH status proportion less than 20%. The right skewed distribution of ideal metrics number in our study was also supported by several recent studies. A report of China Kadoorie Biobank described the distribution of six lifestyle factors and 26% of participants have 0-1 optimal lifestyle factors. However, only 1% of participants have an optimal status for 5-6 lifestyle factors. [5] The Singapore Chinese Health Survey also indicated the right skewed distribution of healthy lifestyles number in 45-74 years old adults. [126] A number of factors could lead to the unsatisfactory CVH status in the general population. One explanation is many countries, especially Asian countries, are experiencing dramatic westernization of lifestyle, such as taking less physical activity and consuming more carbohydrates, which could act as barriers to the CVH improvement. [127, 128] In addition, several studies suggested that the primordial prevention efforts of CVD, measures to prevent the appearances of CVD risk factors, were most effective if performed among infants and children. [129, 130] However, the population-wide CVD primordial prevention efforts, starting from the early phase of life, were extremely scarce worldwide, [131] which precluded us from gaining the maximum cardiovascular benefits. Furthermore, given that the CVH metrics were internally correlated [132, 133] and had a combined effect on CVD risk, finding an appropriate multicomponent intervention strategy may effectively alter the distribution of CVD risk factors. Although we have identified a range of population-based intervention strategies, including media and education campaigns, labeling and consumer information, taxation, school and workplace approaches, community environmental changes, and direct restrictions, [134] it is still unclear the combined effects of these interventions on metrics distribution, which need further explorations.

Another striking finding of our study was the sex, age, regional and study period variations in the ideal CVH metrics and the overall CVH status. It appeared that males and older adults displayed lower frequencies in the overall ideal CVH status, as well as ideal status of most CVH metrics, and higher frequencies in the overall poor CVH status than did the females and young adults. The sex and age inequalities in CVD risk factors distribution were also noticed in recent reports. [135, 136] Nevertheless, cardiovascular benefits of the favorable CVH metrics applied to all sex and age-specific populations. [6, 84, 113, 137] In addition, the ideal CVH status was less than 30% in all sex and age subgroups, which further emphasized the urgent need for primordial prevention of CVD risk factors in the whole population. For geographical variations, it seems that Asians had better CVH status compared to those from Europe and North America, whereas we cannot draw a conclusion due to the limited studies in each subgroup. The possible regional variations in exposure to CVD influencing factors were also suggested elsewhere. [138] Of concern is very limited studies were conducted in South America, Oceania and Africa, it is crucial to conduct more studies in those regions to inform the local policy makers the magnitude of the public health problem. One promising finding of our study was the improvement of the overall CVH and most metrics over study time. However, we could not predict whether the AHA's goal of improving the overall CVH by 20% will be attainable in 2020. [139] A report using NHANES data predicted that the overall CVH status would improve by 6% by 2020 and, therefore, we call for more efforts to measure the progress of CVH improvement and work out a schedule for the coming few years.

One striking strength of our study was it is the first meta-analysis that calculated the pooled prevalence estimates of the ideal status for the seven CVH metrics as well as the overall poor and ideal CVH status. Second, our study should provide reliable estimates as we have a relatively large sample size. We included 75 studies for the prevalence estimates of the ideal CVH metrics, yielding over 1.8 million participants. For the overall poor and ideal CVH status, we included over fifty studies and more than 0.9 million subjects. Third, we took the effects of metrics misclassification, a potential confounder, into consideration by restricted the studies followed AHA's guideline in the second model. Finally, we conducted subgroup analyses based on age, sex, region, and survey time.

Our study, however, has several limitations. First, there were significant between-study variances and age, sex, region and survey time were unable to explain the heterogeneity. Other factors, such as socioeconomic status and genetic elements, may contribute to the variations and we were unable to explore their effects due to limited data. The included studies had different designs, screening instruments and trainee demographics, which may also contribute to the heterogeneity. Second, we were not able to provide accurate comparisons of the CVH between geographical regions, as there were very limited reports in some regions, like South America, Africa, and Oceania. Third, publication bias tests were significant for the prevalence of ideal BMI, dietary pattern, as well as the proportions of the overall poor and ideal CVH status. The imputation of potentially missing studies, however, displayed similar results and, thus, the potential publication bias has little impact on conclusions. In addition, some studies did not strictly follow the metric definitions of AHA and the phenomenon was especially obvious for dietary pattern and physical activity, which may preclude direct comparisons between studies and lead to loss of information.

Conclusion

In summary, the findings of this study displayed the low prevalence of ideal CVH status. Among the seven CVH metrics, ideal status was most prevalent for smoking and least observed for dietary pattern. Generally, females and young adults displayed better CVH status than males and older adults. There also existed some regional variations in the ideal CVH metrics and the overall CVH status. Current evidence also indicated an improvement of the CVH status over time and more efforts are warranted to keep on monitoring the CVH status trend. Additionally, we should initiate multiple high-quality interventions to improve the population-wide CVH status globally.

Author contribution statement

YP and ZW designed the study; YP and SC did the literature search, acquisition of data, and risk of bias assessment; YP and ZY involved statistical analysis; YP drafted the manuscript; SC, ZY, and ZW critical revised the manuscript; YP, SC, ZY, and ZW final approved the manuscript.

Conflicts of interest

All authors declared no conflict of interest.

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Chapter 3 – The CVH status and CVD/IHD risk in adults worldwide

Since the release of the AHA’s Impact Goals, a number of studies have explored the separate and combined effects of Life’s Simple 7 on CVD/IHD risk. The magnitude of the association between Life’s Simple 7 and CVD/IHD risk is unclear. Additionally, the sex and age variations of the strength of association were inconclusive. Measuring the CVH status on CVD/IHD risk has significant implications on the CVD/IHD prevention strategies. This chapter summarized the findings from relevant studies using a systematic review and it addressed the research objective 2 of the thesis.

The association between cardiovascular health metrics and risk of cardiovascular disease in adults: A systematic review

Abstract

Our study was to investigate the association between the seven CVH metrics and CVD risk in adults by conducting a systematic review. We searched PubMed, Embase, Cochrane Central Register of Controlled Trials, and reference lists of relevant articles for cross-sectional or cohort studies published between January 1, 2010, and June 10, 2018. 27 studies, 22 cohort and 5 cross-sectional studies, were included in our study. We observed the higher number of ideal CVH metrics was associated with a substantial reduction in CVD risk and they displayed a dose-response pattern. The individual effects of the CVH metrics on different types of CVD are inconsistent. There exist some age and sex variances in the association magnitude. Promoting the CVH status, even minor improvement, could benefit CVD risk reductions. The association between individual metrics and CVD, especially some CVD types, still need further explorations.

Keywords: cardiovascular health metrics; cardiovascular disease; systematic review

Introduction

CVD is still one of the major health burdens worldwide. It has been estimated that CVD accounted for 32.1% of all deaths globally in 2015. [140] While, several studies have indicated that the majority of CVD burden can be explained by modifiable risk factors, like physical activity, BMI and smoking. [5, 6] In 2010, the AHA outlined the seven CVH metrics, including smoking, BMI, physical activity, dietary pattern, TC, BP, and FPG to define and measure the CVH status in the general population. [7] A number of studies have explored the individual and combined effects of those metrics on the risk of CVD and several systematic reviews and meta-analyses have indicated the negative relationship between the number of ideal CVH metrics and CVD risk in adults. [11, 14, 141] However, they ignored several studies that were cross-sectional design and chosen certain types of CVD as outcomes, like heart failure (HF) and atrial fibrillation (AF). In addition, they only summarized articles that were published before February 2017 and several studies have been published since then.

Our study aimed to synthesize data on both the individual and combined associations between the CVH metrics and CVD risk in adults. We also explored the possible age and sex variations in the strength of the associations.

Methods

Data sources and study selection

Since the AHA's guideline was released in early 2010, we searched relevant studies published between January 1, 2010, and June 10, 2018, using PubMed, Embase, and the Cochrane Central Register of Controlled Trials. Moreover, we manually reviewed references of selected articles and citations of the AHA's guideline. [7] There were no language restrictions. The detailed search strategies were provided in **Table 3.1**.

Table 3.1 Searching details of the systematic review.

Database	Search strategy
PubMed	# 1 (((("cardiovascular health") OR "CVH") OR "Life's Simple 7") OR "Life Simple 7") OR "LS7"
	# 2 (("American Heart Association"[MeSH Terms]) OR "American Heart Association") OR "AHA"
	# 3 ("adult"[MeSH Terms]) OR "adult"
	# 4 ((("cardiovascular diseases"[MeSH Terms]) OR "cardiovascular diseases") OR "cardiovascular disease") OR "CVD"
	#5 #1 AND #2 AND #3 AND #4
Embase	# 1 'cardiovascular health'/exp OR 'cardiovascular health' OR 'CVH' OR 'life* simple 7' OR 'life simple 7' OR 'LS7'
	# 2 'american heart association' OR 'aha'
	# 3 'adult'/exp OR 'adult'
	# 4 'cardiovascular disease'/exp OR 'cardiovascular disease' OR 'cvd'
	# 5 #1 AND #2 AND #3 AND #4
Cochrane Central Register of Controlled Trials	#1 "cardiovascular health" OR "CVH" OR "Life's Simple 7" OR "Life Simple 7" OR "LS7"
	#2 MeSH descriptor: [American Heart Association] explode all trees OR "American Heart Association" OR "AHA"
	#3 MeSH descriptor: [Adult] explode all trees OR "adult"
	#4 MeSH descriptor: [Cardiovascular diseases] explode all trees OR "Cardiovascular diseases" OR "Cardiovascular disease" OR "CVD"
	#5 #1 AND #2 AND #3 AND #4

To be included, the studies should in accordance with the following criteria: (a) cross-sectional or cohort studies; (b) measured the seven CVH metrics; (c) provided the effect sizes and 95% CIs of the associations between the CVH metrics and CVD prevalence, incidence, or mortality; and (d) all the participants were aged 18 years or over. We excluded reviews, conference abstracts, letters, case reports, and editorials. Two investigators (YP and ZW) performed the article screening and selection and disagreements were resolved by consensus.

Data extraction and risk of bias assessment

For each included article, we extracted first author, year of publication, name of the study, country where the study was conducted, study type, study period, number of participants, age range and male percentage of the participants, and outcomes. We directly contacted authors for more details if relevant data were unclear in the paper. We used the Newcastle-Ottawa Scale (NOS) to evaluate the quality of the included studies. A 9 stars and an adapted 10 stars scale were used for cohort and cross-sectional studies, respectively. [142] Two authors (YP and ZW) independently extracted the information and assessed the study quality and disagreements were settled down by discussion.

Statistical analysis

We summarized the effect sizes, including hazard ratio, odds ratio (OR), and relative risk, and 95% CIs between the number of ideal metrics/ideal status of individual metrics and CVD related outcomes. The significance of associations was determined by the two-sided *P* values, with 0.05 as the cut-off point. As there are limited studies for each outcome and different definitions of outcomes, we did not calculate the pooled effect sizes and 95% CIs.

Results

Study characteristics

A total of 27 studies [12, 27, 29, 30, 35, 36, 42, 63, 69, 84, 85, 91, 105, 113, 143-155] were included in our study and **Figure 3.1** shows the details of the literature search. Around half of the studies were conducted in the United States (48%, 13/27). Of the 27 included studies, 22 (81.5%) were cohort studies and the remaining 5 (18.5%) were cross-sectional studies. Overall, the quality of the included studies was high according to the NOS (≥ 7 stars). The general characteristics of the included studies were listed in **Table 3.2**.

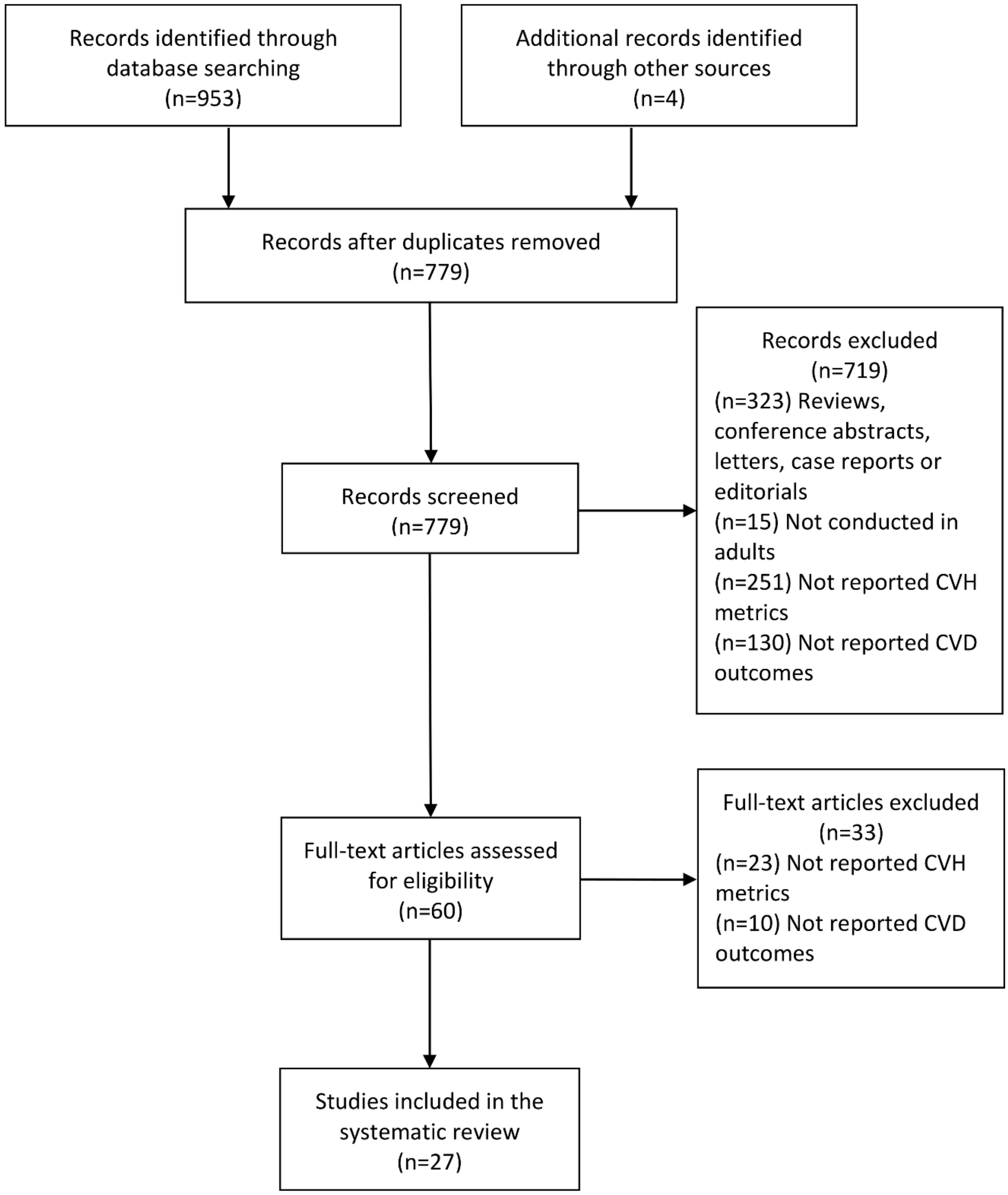

Figure 3.1 Flow chart of study selection. Abbreviations: CVH, cardiovascular health; CVD, cardiovascular disease.

Table 3.2 General characteristics of the included studies.

First author, publication year	Name of study	Location	Study type	Study period	Total participants	Age range (years)	% Male	Outcomes	NOS
Folsom AR, 2011 [12]	ARIC	United States	Cohort	1987-1989	12744	45-64	44	CVD incidence	8
Artero EG, 2012 [27]	ACLS	United States	Cohort	1987-1999	11993	20-88	76	CVD mortality	8
Wu S, 2012 [29]	KaiLuan Study	China	Cohort	2006-2007	91698	18-98	79	CVD incidence	8
Yang Q, 2012 [30]	NHANES	United States	Cohort	1988-1994	16215	≥ 20	48	CVD mortality IHD mortality	9
Kim JY, 2013 [35]	Seoul Male Cohort Study	South Korea	Cohort	1993	12538	40-59	100	CVD mortality	8
Kulshreshtha A, 2013 [36]	REGARDS	United States	Cohort	2003-2007	22914	≥ 45	42	Stroke incidence	8
Zhang Q, 2013 [42]	KaiLuan Study	China	Cohort	2006-2007	91698	18-98	79	Stroke incidence	8
Olson NC, 2015 [63]	REGARDS	United States	Cohort	2003-2007	27402	≥ 45	45	VTE incidence	8
Foraker RE, 2016 [69]	WHI	United States	Cohort	1992	115306	50-79	0	CVD incidence	8
Gaye B, 2017 [84]	Three-City Study	France	Cohort	1999-2001	7371	≥ 65	37	CVD mortality CHD incidence Stroke incidence	8
Gaye B, 2017 [85]	PRIME	France Ireland	Cohort	1991-1993	9312	50-59	100	CHD incidence Stroke incidence	8
Ogunmoroti O, 2017 [91]	MESA	United States	Cohort	2000-2002	6506	45-84	47	HF incidence	8
Han C, 2018 [105]	China-PAR	China	Cohort	1988 2000-2001 2007-2008	93987	≥ 20	40	CHD incidence Stroke incidence	9

Zhou L, 2018 [113]	China-USA	China	Cohort	1981	938	35-59	50	CVD mortality CVD incidence CHD incidence	7
Dong C, 2012 [143]	NOMAS	United States	Cohort	1993-2001	2981	≥ 40	36	CVD incidence MI incidence Stroke incidence CVD mortality	7
Ford ES, 2012 [144]	NHANES	United States	Cohort	1999-2002	7622	≥ 20	48	CVD mortality	9
Zhang Q, 2013 [145]	APAC	China	CS	2010-2011	5412	≥ 40	60	ICAS prevalence	9
Liu Y, 2014 [146]	KaiLuan Study	China	Cohort	2006-2007	95429	18-98	80	CVD mortality	8
Folsom AR, 2015 [147]	ARIC	United States	Cohort	1987-1989	13462	45-64	45	HF incidence	8
Guo L, 2016 [148]	NA	China	CS	2012-2013	11417	≥ 35	46	Stroke prevalence	9
Lachman S, 2016 [149]	EPIC-Norfolk	United Kingdom	Cohort	1993-1997	10043	39-79	44	CVD incidence	8
Ommerborn MJ, 2016 [150]	JHS	United States	Cohort	2000-2004	4702	≥ 20	36	CVD incidence	7
Peng Y, 2017 [151]	AHS	Australia	CS	2011-2012	7499	≥ 18	44	CVD prevalence	8
Peng Y, 2017 [152]	AHS	Australia	CS	2011-2012	7499	≥ 18	44	IHD prevalence	8
Yang Y, 2017 [153]	NA	China	CS	2013-2014	4477	40-82	49	AF prevalence	8
Garg PK, 2018 [154]	ARIC	United States	Cohort	1987-1989	13182	45-64	44	AF incidence	8
Garg PK, 2018 [155]	REGARDS	United States	Cohort	2003-2007	9576	≥ 45	43	AF incidence	8

Abbreviations: NOS, Newcastle-Ottawa Scale; ARIC, Atherosclerosis Risk in Communities; CVD, cardiovascular disease; ACLS, Aerobics Centre Longitudinal Study; NOMAS, Northern Manhattan Study; MI, myocardial infarction; NHANES, National Health and Nutrition Examination Survey; IHD, ischemic heart disease; REGARDS, Reasons for Geographic and Racial Differences in Stroke; APAC, Asymptomatic Polyvascular Abnormalities Community; CS, cross-sectional; ICAS, intracranial arterial stenosis; HF, heart failure; VTE, venous thromboembolism; WHI, Women's Health Initiative; NA, not available; JHS, Jackson Heart Study; CHD, coronary heart disease; PRIME, Prospective Epidemiological Study of Myocardial Infarction; MESA, Multi-Ethnic Study of Atherosclerosis; AHS, Australian Health Survey; AF, atrial fibrillation.

Number of ideal CVH metrics and CVD risk

Table 3.3 listed the results of associations between number of ideal metrics and CVD related outcomes. In all studies, persons with higher numbers of ideal CVH metrics had a lower risk of overall CVD mortality, [27, 30, 35, 84, 113, 143, 144, 146] incidence, [12, 29, 69, 113, 143, 150] and prevalence [151] than did those with fewer ideal CVH metrics. Compared with persons in the lowest ideal metrics categories, persons in the highest categories had 42% to 90%, 59% to 89%, and 66% reduction in the risk of CVD mortality, incidence, and prevalence, respectively.

Several studies have explored the association between ideal CVH metrics number and IHD mortality, [30] IHD prevalence, [152] CHD incidence, [84, 85, 105, 113] stroke incidence, [36, 42, 84, 85, 105, 113, 143] and stroke prevalence [148] and they all demonstrated an inverse association. Participants in the highest categories had 70%, 78% and 42%-73% reduced risk of IHD mortality, IHD prevalence, and CHD incidence compared with those in the lowest categories. For stroke incidence and prevalence, the odds had reduced by 55%-83% and 77%, respectively.

A few studies also indicated that the greatest number of the ideal CVH metrics could eliminate 84% of myocardial infarction incidence, [143] 64% of intracranial artery stenosis (ICAS) prevalence, [145] 83%-85% of HF incidence, [91, 147] 50% of AF incidence, [154] and 56% of AF prevalence [153] compared to those with fewest number of the ideal CVH metrics.

In addition, several studies have focused on the sex and age disparities in the association magnitude. It has been reported that the effects of the ideal CVH metrics number are more pronounced among females than among males regarding the incidence of overall CVD [29, 150] and stroke. [42] However, the effects are more obvious in males in females for ICAS prevalence [145] and HF incidence. [91] Two studies have found the association strength is more significant in younger adults compared to that in older adults for stroke [42] and HF incidence, [91] whereas a study observed an opposite association for ICAS prevalence. [145]

Individual CVH metrics and CVD risk

Several studies have explored the effects of the individual CVH metrics on the risk of CVD mortality, [27, 30, 35, 144, 146] CVD incidence, [29, 149] CVD prevalence, [151] CHD incidence, [105] IHD mortality, [30] IHD prevalence, [152] stroke incidence, [36, 42, 105] stroke prevalence, [148] HF incidence, [91] ICAS prevalence, [145] venous thromboembolism (VTE) incidence, [63] AF incidence, [155] and AF prevalence. [153] The detailed information on the association was shown in **Table 3.4**.

Table 3.3 The associations between the number of ideal CVH metrics and CVD-related outcomes.

First author, publication year	Outcome	Number of ideal metrics	Effect size (95% CI)
Folsom AR, 2011 [12]	CVD incidence	0	Referent
		1	0.65 (0.55-0.77)
		2	0.46 (0.39-0.54)
		3	0.34 (0.28-0.40)
		4	0.24 (0.20-0.29)
		5	0.18 (0.14-0.23)
		6	0.11 (0.07-0.17)
Artero EG, 2012 [27]	CVD mortality	0-2	Referent
		3-4	0.45 (0.27-0.77)
		5-7	0.37 (0.15-0.95)
Wu S, 2012 [29]	CVD incidence	0	Referent
		1	0.88 (0.68-1.13)
		2	0.63 (0.49-0.81)
		3	0.47 (0.36-0.60)
		4	0.34 (0.26-0.44)
		5	0.24 (0.17-0.34)
		6-7	0.18 (0.08-0.40)
Yang Q, 2012 [30]	CVD mortality	0-1	Referent
		2	0.73 (0.59-0.91)
		3	0.56 (0.44-0.71)
		4	0.52 (0.41-0.66)
		5	0.44 (0.30-0.65)
		6-7	0.24 (0.13-0.47)
	IHD mortality	0-1	Referent
		2	0.74 (0.55-1.00)
		3	0.54 (0.40-0.72)
		4	0.51 (0.37-0.72)
		5	0.43 (0.26-0.72)
		6-7	0.30 (0.13-0.68)
Kim JY, 2013 [35]	CVD mortality	0-2	Referent

		3	0.77 (0.46-1.29)
		4	0.46 (0.27-0.76)
		5	0.31 (0.18-0.53)
		6-7	0.10 (0.03-0.29)
Kulshreshtha A, 2013 [36]	Stroke incidence	0	Referent
		1	0.70 (0.42-1.19)
		2	0.67 (0.40-1.13)
		3	0.53 (0.31-0.90)
		4	0.40 (0.23-0.73)
		5	0.50 (0.25-1.00)
		6	0.34 (0.08-1.52)
Zhang Q, 2013 [42]	Stroke incidence	0	Referent
		1	0.92 (0.69-1.23)
		2	0.69 (0.52-0.92)
		3	0.52 (0.39-0.68)
		4	0.38 (0.28-0.51)
		5	0.27 (0.18-0.40)
		6-7	0.24 (0.11-0.54)
Foraker RE, 2016 [69]	CVD incidence	0-1	6.83 (5.83-8.00)
		2	4.43 (3.91-5.03)
		3	2.77 (2.45-3.13)
		4	2.06 (1.83-2.33)
		5	1.46 (1.29-1.66)
		6-7	Referent
Gaye B, 2017 [84]	CVD mortality	0-2	Referent
		3-4	0.85 (0.69-1.03)
		5-7	0.54 (0.29-0.98)
	CHD incidence	0-2	Referent
		3-4	0.63 (0.52-0.77)
		5-7	0.27 (0.13-0.57)
	Stroke incidence	0-2	Referent
		3-4	0.82 (0.64-1.06)

		5-7	0.45 (0.20-1.03)
Gaye B, 2017 [85]	CHD incidence	0-2	Referent
		3-4	0.58 (0.49-0.68)
		5-7	0.28 (0.17-0.46)
	Stroke incidence	0-2	Referent
		3-4	0.84 (0.58-1.21)
		5-7	0.24 (0.06-0.98)
Ogunmoroti O, 2017 [91]	HF incidence	0-1	Referent
		2	0.93 (0.60-1.44)
		3	0.68 (0.45-1.05)
		4	0.52 (0.33-0.83)
		5	0.34 (0.18-0.63)
		6-7	0.15 (0.04-0.65)
Han C, 2018 [105]	CHD incidence	0-2	Referent
		3	0.72 (0.57-0.90)
		4	0.52 (0.42-0.65)
		5	0.48 (0.38-0.61)
		6	0.36 (0.27-0.49)
		7	0.35 (0.22-0.58)
	Stroke incidence	0-2	Referent
		3	0.87 (0.76-0.99)
		4	0.71 (0.62-0.81)
		5	0.56 (0.49-0.65)
		6	0.45 (0.39-0.53)
		7	0.21 (0.15-0.28)
Zhou L, 2018 [113]	CVD mortality	0-2	Referent
		3	0.50 (0.19-1.31)
		4-7	0.43 (0.16-1.16)
	CVD incidence	0-2	Referent
		3	0.59 (0.33-1.04)
		4-7	0.24 (0.12-0.47)
	CHD incidence	0-2	Referent

		3	0.42 (0.10-1.84)
		4-7	0.58 (0.15-2.31)
	Stroke incidence	0-2	Referent
		3	0.58 (0.32-1.08)
		4-7	0.17 (0.08-0.38)
Dong C, 2012 [143]	CVD incidence	0-1	Referent
		2	0.73 (0.60-0.89)
		3	0.61 (0.50-0.76)
		4	0.49 (0.38-0.63)
		5-7	0.41 (0.26-0.63)
	MI incidence	0-1	Referent
		2	0.78 (0.54-1.12)
		3	0.57 (0.38-0.84)
		4	0.53 (0.33-0.85)
		5-7	0.16 (0.05-0.52)
	Stroke	0-1	Referent
		2	0.71 (0.51-0.99)
		3	0.60 (0.42-0.84)
		4	0.49 (0.31-0.76)
		5-7	0.43 (0.21-0.91)
Ford ES, 2012 [144]	CVD mortality	0	Referent
		1	0.40 (0.15-1.09)
		2	0.46 (0.17-1.22)
		3	0.25 (0.09-0.67)
		4	0.27 (0.10-0.72)
		5-7	0.12 (0.03-0.57)
Zhang Q, 2013 [145]	ICAS prevalence	0-1	Referent
		2	0.76 (0.58-0.99)
		3	0.55 (0.43-0.72)
		4	0.49 (0.37-0.65)
		5	0.43 (0.31-0.61)
		6-7	0.36 (0.22-0.62)

Liu Y, 2014 [146]	CVD mortality	0-1	Referent
		2	0.88 (0.69-1.12)
		3	0.71 (0.55-0.90)
		4	0.58 (0.44-0.77)
		5-7	0.61 (0.41-0.89)
Folsom AR, 2015 [147]	HF incidence	0	Referent
		1	0.75 (0.65-0.85)
		2	0.52 (0.43-0.64)
		3	0.39 (0.31-0.48)
		4	0.27 (0.22-0.34)
		5	0.17 (0.13-0.23)
		6	0.17 (0.11-0.28)
Guo L, 2016 [148]	Stroke incidence	1	4.44 (1.66-11.79)
		2	4.03 (1.62-10.00)
		3	3.60 (1.46-8.85)
		4	3.27 (1.33-8.03)
		5	2.26 (0.91-5.61)
		6	2.24 (0.88-6.59)
		7	Referent
Ommerborn MJ, 2016 [150]	CVD incidence	0-1	Referent
		2	0.66 (0.49-0.88)
		3	0.45 (0.32-0.64)
		4-7	0.29 (0.17-0.52)
Peng Y, 2017 [151]	CVD prevalence	0-2	Referent
		3-4	0.67 (0.56-0.81)
		5-7	0.34 (0.22-0.55)
Peng Y, 2017 [152]	IHD prevalence	0-2	Referent
		3-4	0.55 (0.39-0.77)
		5-7	0.22 (0.03-1.96)
Yang Y, 2017 [153]	AF prevalence	0-2	Referent
		3-4	0.41 (0.22-0.80)
		5-7	0.44 (0.20-0.98)

Garg PK, 2018 [154]	AF incidence	0-1	Referent
		2-3	0.75 (0.68-0.83)
		4-7	0.50 (0.44-0.56)

Abbreviations: CVH, cardiovascular health; CVD, cardiovascular disease; CI, confidence interval; IHD, ischemic heart disease; CHD, coronary heart disease; HF, heart failure; MI, myocardial infarction; ICAS, intracranial arterial stenosis; AF, atrial fibrillation.

Table 3.4 The associations between the seven CVH metrics and CVD-related outcomes.

Outcomes	Smoking	BMI	Physical activity	Dietary pattern	TC	BP	FPG
CVD mortality [27,30,35,144,146]	+/-	-	+/-	-	+/-	+	+/-
CVD incidence [29,149]	+	+	+/-	+/-	+	+	+
CVD prevalence [151]	+	+	+	-	+	+	+
CHD incidence [105]	+	-	+	-	+	+	+
IHD mortality [30]	+	-	-	+	-	-	+
IHD prevalence [152]	-	+	+	-	+	-	-
Stroke incidence [36,42,105]	+	+/-	+/-	+/-	+/-	+	+
Stroke prevalence [148]	-	+	NA	+	+	+	+
HF incidence [91]	+	+	+	-	-	+	+
ICAS prevalence [145]	+	-	-	-	+	+	+
VTE incidence [63]	-	+	+	-	-	-	-
AF incidence [155]	-	+	-	-	-	+	-
AF prevalence [153]	-	-	+	-	-	-	-

Abbreviations: CVH, cardiovascular health; CVD, cardiovascular disease; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CVD, cardiovascular disease; CHD, coronary heart disease; IHD, ischemic heart disease; NA, not available; HF, heart failure; ICAS, intracranial arterial stenosis; VTE, venous thromboembolism; AF, atrial fibrillation.

"+", "-" and "+/-" indicate significant, non-significant, and inconsistent associations, respectively. The association between physical activity and stroke prevalence was not available because all the participants were having ideal physical activity status.

Two studies have provided the sex and age-specific associations between those metrics and ICAS [145] and AF [153] prevalence. As a result, smoking is significant ICAS risk factors in males and older adults (≥ 60 years) instead of in females and younger adults (40-59 years). Elevated TC was a significant ICAS risk factor in males, but the association disappeared in females. The other metrics have similar effects on ICAS prevalence for sex and age subgroups. For AF prevalence, sufficient physical activity could significantly reduce the AF risk for females and older adults (60-82 years), whereas it is not significant for males and younger adults (40-59 years). Ideal dietary pattern could lead to AF prevalence reduction in males instead of in females and optimal FPG could reduce AF risk in younger adults rather than in older adults. There are not apparent age and sex disparities for other metrics.

Discussion

Our study, based on included cohort and cross-sectional studies, reached a consistent conclusion that greater number of the ideal CVH metrics was associated with significant risk reductions in not only overall CVD but also in specific types of CVD. For each CVH metric, there exist association magnitude variances with different CVD outcomes.

The findings of an inverse relationship between the ideal CVH metrics number and CVD risk were consistent with previous reports. A recent meta-analysis indicated that, compared to the subjects in the lowest CVH categories, those in the highest CVH categories have 70%, 78%, and 67% reduced risk of CVD mortality, CVD events, and stroke events. [148] In a Chinese cohort study with nearly 0.5 million participants, having an optimal status of 5 or 6 lifestyle factors, compared to having 0 optimal lifestyle factor, were associated with 63%, 50%, and 50% reduced risk of major coronary heart events, IHD events, and ischemic stroke events, respectively. [5] A cohort study, conducted in 84537 women in the United States, observed that 4 lifestyle factors (smoking, dietary pattern, BMI, and physical activity) could explain 77% of HF risk. [156] Furthermore, we found a dose-response fashion between the number of ideal CVH metrics and CVD risk in most included studies, indicating even minor improvement in the CVH status could result in benefits of CVD risk. Thus, initiating multiple lifestyle interventions in the general population level could bring about substantial improvement in the CVH distribution.

Another striking finding is individual metrics displayed different association strength regarding different CVD outcomes. For example, ideal BMI could lead to a significant reduction in overall CVD incidence, [29, 149] while the association disappeared for AF prevalence. [153] One possible explanation is the risk factor profile disparities for various types of CVD. A recent meta-analysis also supports the hypothesis, which identified processed meat intake as a significant risk factor of

CHD instead of stroke. [157] Another possible explanation is the limited available data, especially for some less prevalent types of CVD. As shown, only less than ten studies have focused on the CVD outcomes other than overall CVD, CHD/IHD, or stroke. While, there are numerous CVD related outcomes, as indicated by the AHA's guideline. [7] Understanding the association between the CVH metrics and those CVDs could facilitate the prevention and treatment of those conditions and, thus, finally reduce the overall CVD burden.

We also observed the sex and age differences in the association between the CVH metrics and CVD risk. The specific sex and age CVD risk factor profiles, which have been suggested by previous studies, may partly account for the phenomenon. The China Kadoorie Biobank Study revealed that the association and contribution of uncontrolled hypertension to vascular mortality were more pronounced in younger adults (35-59 years) than in older adults (60-79 years). [158] A review indicated that the effects of smoking and diabetes on CHD risk were greater in women than in men, whereas the impact of elevated BMI was more obvious in men instead. [159] Given the situation, studies are needed on how to implement sex and age specific prevention and treatment strategies to maximize the CVH benefits.

One strength of our study is the inclusion more recent studies on the relationship between AHA's CVH metrics and CVD outcomes. Another advantage is the exploration of age/sex distinctions in the association pattern. Our study also has several limitations. First, there exists some variances in the population characteristics, in terms of age, sex, and socioeconomic status, as well as measurements of the CVH metrics and outcomes. Second, some other lifestyle factors, like alcohol intake, were not included in our analysis. Third, there are significant heterogeneity in the measurements of outcomes and metrics, which precluded the calculation of pooled effect sizes. For example, some studies strictly followed the AHA's definition of dietary pattern, [69, 143, 160] while others only included a few components of the AHA's definition. [30, 151]

Conclusion

Our study demonstrated that higher number of the ideal CVH metrics was associated with substantial CVD reductions. We also observed that, for each metric, the effect magnitudes on different CVD outcomes varied. The impacts of the CVH metrics on some less prevalent types of CVD are still poorly understood.

Acknowledgements

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Chapter 4 – The CVH status in Australian adults

As described in Chapter 2, the overall CVH is poor worldwide and there existed disparities regarding the proportion of ideal status for the seven metrics. In addition, we also observed regional variations in the CVH status. However, very few studies have explored the CVH status in Australian adults. Since CVD is a great health burden in Australia, understanding the CVH status in Australian adults has significant benefits for health promotion. In this chapter, we measured the CVH status in Australian adults using the core sample of the 2011-2012 AHS. Furthermore, we conducted subgroup analyses by sex and age. The chapter addressed the research objective 3 of the thesis.

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Zhiqiang Wang	Conception and design (20%) Reviewing of article (60%)

Cardiovascular health status among Australian adults

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Abstract

Background: The AHA committee recently set a guideline to define and monitor the CVH status. The current study is to estimate the CVH status among Australian adults using the guideline.

Methods: We used data from a nationally representative sample of 7499 adults (age ≥ 18 years) from the 2011-2012 AHS. We applied the modified AHA's definition to estimate the ideal proportions of the seven metrics and the overall CVH status.

Results: Ideal status was most prevalent for FPG (83.6%) and least observed for dietary pattern (4.8%). The estimated percentages of the overall poor (having 0-2 ideal metrics) and ideal CVH (having 5-7 ideal metrics) were 39.85% and 18.72% in Australian adults. There exist some age and sex variations for the ideal status of individual metric and the overall CVH.

Conclusion: The percentage of the overall ideal CVH in Australian adults is extremely low. Public health policies should be implemented to improve the population-wide CVH status in Australia.

Keywords: cardiovascular health, Australian adults, cross-sectional study, risk factors

Introduction

Although a recent report has indicated the CVD mortality declined, [161] CVD is still a leading cause of deaths over time. [19] In 2013, CVD contributed to > 17 million deaths globally, with an age-standardized death rate of 293.2 per 100000. [19] Previous studies have identified the substantial role of modifiable factors in CVD prevention. Among 42847 men aged 40 to 75, Chiuve *et al* [137] defined 5 healthy lifestyle factors, including being a non-smoker, having a BMI < 25 kg/m^2, taking moderate to vigorous physical activity for at least 30 minutes daily, consuming 5-30 g of alcohol daily, and having a healthy diet. After 16 years of follow-up, each of the five factors was associated with a substantially lower risk of CHD incidence. In addition, 62% of coronary events may have been prevented by better adherence to these lifestyle factors. [137] In the NHANES, participants with untreated BP <120/<80 mmHg and untreated glycated hemoglobin < 5.7% had 36% and 29% lower risk of CVD mortality, respectively. In this context, the AHA has set the following goals for 2020: “by 2020, to improve the CVH of all Americans by 20% while reducing deaths from CVD and stroke by 20%”. [7] In the meanwhile, the AHA identified seven modifiable metrics, called Life’s Simple 7, to define and monitor the CVH status and prompt the achievement of the 2020 goals. Life’s Simple 7 consisted of BMI, physical activity and dietary pattern as health behaviors, TC, BP and FPG as health factors and smoking as both health behavior and health factor. [7] Several recent studies have observed the separate and combined effects of Life’s Simple 7 on the reductions of CVD mortality, [30, 144] incidence, [150] and presence. [162] There are also a number of reports on the CVH status. [49, 55, 58, 163]

Australia is also suffering from the enormous burden of CVD in terms of death, hospitalization, and incidence. CVD attributed to 46106 deaths, nearly one third of the total deaths, among Australians in the year of 2009. [2] In Australia from 2009 to 2010, there were almost 0.5 million hospitalizations with a principal diagnosis of CVD. [2] It has reported that one out of five Australians aged 45 to 74 years had a high risk of CVD event in the subsequent 5 years. [164] Another large-scale study based on Australians aged 45 or over observed that 22% of participants have a prior history of CVD. [3] Therefore, obtaining the national data for the CVH status is crucial in Australia, while such data has been limited until now.

In the current study, we used data from a nationally representative survey, the 2011-2012 AHS, to evaluate the status of the CVH in Australian adults. We hypothesized that the Australian adults are suffering from the poor CVH status. Young and females may have better CVH status.

Methods

Study design and subjects

The current study was based on the core sample of the 2011-2012 AHS, which was a national wide and population-based combined sample of three surveys: National Health Survey (NHS), National Nutrition and Physical Activity Survey (NNPAS), and National Health Measures Survey (NHMS). Australian Bureau of Statistics (ABS) organized the three surveys. NHS and NNPAS used complex, multistage and probability sampling design to select usual residents from private dwellings in urban and rural areas of all states and territories in Australia, covering about 97% of the people living in Australia. Overseas visitors staying or intending to stay in Australia for 12 months or more were also in scope. Households in Very Remote areas of Australia and discrete Aboriginal and Torres Strait Islander communities were excluded. All participants aged 12 or over and aged 5 or over in both NHS and NNPAS were asked to voluntarily provide fasting blood samples and urine samples, which constituted the NHMS. The 2011-2012 AHS core sample combined subjects from NHS and NNPAS and contained variables that co-existed in the two surveys. Biomedical results from NHMS were also included. The core sample consisted of 24910 adults (≥ 18 years old) and the present study restricted those who voluntarily participated in both TC and FPG tests (n=7499), yielding an overall response rate of 30.1%.

All participants provided written informed consent and our study was approved by The School of Medicine Low Risk Ethical Review Committee at the University of Queensland (approval number 2016-SOMILRE-0161).

Data collection

Trained interviewers obtained the NHS and NNPAS information through face-to-face Computer Assisted Personal Interview. For the 24-hour dietary recall collection, Computer Assisted Telephone Interview was used. Participants provided their biomedical samples to the convenient collection centers and Sonic Healthcare processed those samples.

Smoking status was based on participants' self-reported currently, ever or never smoke. Height and weight were measured during the interview and BMI was computed as weight in kilograms divided by height in meters squared. ABS staff used a series of questions to obtain the physical activity that the subjects undertook in the last week and calculated the total minutes of moderate and vigorous physical activity. To assess the fruits and vegetables consumption, participants were asked to report the number of vegetables and fruits serves they usually ate each day. For BP, interviewers undertook two BP readings using an automated BP monitor in which systolic and diastolic pressures were displayed. If the difference between the readings was greater than 10 mm Hg, for either the diastolic or systolic, a third reading was taken. If there were three readings, the average of the second and third readings was used for the analysis. For those with one and two readings, the first and second readings were utilized, respectively. Serum TC was measured by using the Cholesterol Oxidase method and analyser Architect ci16200. Additionally, participants were asked whether taking lipid-lowing medications or not. FPG was assessed by using Hexokinase method and analyser Integra 800.

Life's Simple 7

We adopted the AHA's definition of Life's Simple 7 based on our dataset structure and the modified definition was detailed in **Table 4.1**. The overall poor and ideal CVH were defined as having 0-2 and 5-7 ideal CVH metrics. [84]

Table 4.1 The modified definition of the CVH metrics in the present study.

Metrics	**Ideal status**	**Unideal status**
Smoking status	Never smokers	Current and former smokers
BMI	< 25 kg/m^2	≥ 25 kg/m^2
Physical activity	≥ 150 min/week moderate or ≥ 75 min/week vigorous or ≥ 150 min/week moderate + vigorous	< 150 min/week moderate, < 75 min/week vigorous and < 150 min/week moderate + vigorous
Dietary pattern	Having met the fruits and vegetables intake requirement defined by 2013 Australian Dietary Guidelines	Having not met the fruits and vegetables intake requirement defined by 2013 Australian Dietary Guidelines
BP	Systolic BP < 120 mm Hg and diastolic BP < 80 mm Hg	Systolic BP ≥ 120 mm Hg and/or diastolic BP ≥ 80 mm Hg
TC	< 200 mg/dL and not taking cholesterol-lowing medication	≥ 200 mg/dL and/or taking cholesterol-lowing medication
FPG	< 100 mg/dL	≥ 100 mg/dL

Abbreviations: CVH, cardiovascular health; BMI, body mass index; BP, blood pressure; TC, total cholesterol; FPG, fasting plasma glucose.

Statistical analysis

We compared the demographic and CVH metrics, except for TC and FPG, between the participants and non-participants using person weight and jackknife method. Proportions and corresponding CIs of ideal status for each metric were calculated in the total population as well as by sex and age, categorized as young adults (ages 18-39 years), middle-aged adults (ages 40-59 years), and older adults (ages ≥ 60 years), subgroups. Proportions and CIs of the number of the ideal CVH metrics from 0 to 7 were also computed in the overall population and subgroups. Participants with available CVH metrics were included in ideal proportion estimates for specific metrics. Participants with complete information on all CVH metrics were included for proportion estimates of the numbers of the ideal CVH metrics. Survey-based chi-square tests were conducted to make comparisons between subgroups. Weights were applied to account for the sampling strategy and represent the overall Australian adults. Since our study based on those with biomedical samples, we used biomedical weights as recommended by ABS. In addition, we used the jackknife method to estimate the sampling error.

All the analyses were performed in the ABS Remote Access Data Laboratory (RADL) and we used Stata version 10.0, which is the available software of RADL. A two-tailed P-value < 0.05 was considered statistically significant.

Results

The comparisons of the characteristics of participants and non-participants are listed in **Table 4.2**. The distributions of the seven CVH metrics in the total population and subgroups are displayed in **Table 4.3**. In the overall population, the weighted proportions of the ideal CVH metrics were as follows: FPG, 83.6%; smoking, 55.6%; TC 45.5%; BP, 44.2%; BMI, 39.2%; physical activity, 26.7%; and dietary pattern 4.8%. Men and women have similar ideal proportions regarding the TC (P = 0.70). A significantly higher proportion of males had ideal physical activity compared with females (P < 0.01). More women than men met the favorable status of the other five metrics (P < 0.01). The distinctions in the ideal proportions of these metrics were also noted across the three age groups. There is an increasing trend regarding the ideal proportion of dietary pattern with aging (P=0.01), whereas the tendency was reversed for the other six metrics (P < 0.01).

Table 4.2 Comparisons of demographics and CVH metrics between participants and non-participants.

Items	Participants (%)*	Non-participants (%)*	*P**
Smoking, ideal	53.3	50.2	< 0.01
BMI, ideal	35.5	38.0	0.01
Physical activity, ideal	24.3	24.3	0.98
Dietary pattern, ideal	5.2	3.9	< 0.01
BP, ideal	40.8	43.0	0.01
Age, < 60 years	68.0	78.7	< 0.01
Sex, male	48.2	49.8	0.07
Education, high	52.2	54.4	0.02
Income, high	50.6	51.7	0.31
Region			< 0.01
Major cities	69.0	72.2	
Inner regional	22.2	17.8	
Other	8.8	10.0	

Abbreviations: BMI, body mass index; BP, blood pressure.
* Weighted prevalence and chi-square tests using person weight.

Table 4.3 Weighted proportions of the CVH metrics in Australian adults.

Metrics	Total		Males		Females		Young		Middle-aged		Older	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Smoking status												
Ideal	3762	55.6 (54.0-57.2)	1420	49.8 (47.7-52.0)	2342	61.1 (58.7-63.5)	1146	64.8 (62.2-67.5)	1375	49.5 (47.1-51.9)	1241	49.0 (46.3-51.8)
Unideal	3737	44.4 (42.8-46.0)	1909	50.2 (48.0-52.3)	1828	38.9 (36.5-41.3)	743	35.2 (32.5-37.8)	1559	50.5 (48.1-52.9)	1435	51.0 (48.2-53.7)
BMI												
Ideal	2395	39.2 (37.3-41.1)	833	32.3 (29.6-35.0)	1562	46.2 (43.7-48.6)	873	53.7 (50.0-57.4)	877	30.9 (28.7-33.1)	645	27.2 (25.0-29.5)
Unideal	4732	60.8 (58.9-62.7)	2388	67.7 (65.0-70.4)	2344	53.8 (51.4-56.3)	916	46.3 (42.6-50.0)	1927	69.1 (66.9-71.3)	1889	72.8 (70.5-75.0)
Physical activity												
Ideal	1774	26.7 (25.2-28.3)	945	32.7 (30.4-35.1)	829	20.9 (18.9-22.9)	630	35.4 (32.3-38.5)	690	23.9 (21.7-26.1)	454	16.6 (14.7-18.5)
Unideal	5721	73.3 (71.7-74.8)	2382	67.3 (64.9-69.6)	3339	79.1 (77.1-81.1)	1257	64.6 (61.5-67.7)	2243	76.1 (73.9-78.3)	2221	83.4 (81.5-85.3)
Dietary pattern												
Ideal	434	4.8 (4.1-5.4)	93	2.1 (1.5-2.6)	341	7.4 (6.2-8.6)	73	3.7 (2.3-5.1)	150	4.5 (3.5-5.5)	211	6.9 (5.7-8.2)
Unideal	7065	95.2 (94.6-95.9)	3236	97.9 (97.4-98.5)	3829	92.6 (91.4-93.8)	1816	96.3 (94.9-97.7)	2784	95.5 (94.5-96.5)	2465	93.1 (91.8-94.3)
BP												
Ideal	2828	44.2 (42.8-45.7)	1047	36.7 (34.3-39.2)	1781	51.6 (49.6-53.6)	1114	61.2 (58.5-63.8)	1120	40.0 (37.6-42.4)	594	21.9 (19.5-24.3)
Unideal	4393	55.8 (54.3-57.2)	2189	63.3 (60.8-65.7)	2204	48.4 (46.4-50.4)	714	38.8 (36.2-41.5)	1713	60.0 (57.6-62.4)	1966	78.1 (75.7-80.5)
TC												
Ideal	2827	45.5 (43.8-47.2)	1259	45.1 (42.8-47.5)	1568	45.8 (43.4-48.2)	1210	66.8 (63.6-69.9)	1036	36.1 (33.3-39.0)	581	23.9 (21.7-26.0)
Unideal	4672	54.5 (52.8-56.2)	2070	54.9 (52.5-57.2)	2602	54.2 (51.8-56.6)	679	33.2 (30.1-36.4)	1898	63.9 (61.0-66.7)	2095	76.1 (74.0-78.3)
FPG												
Ideal	5939	83.6 (82.5-84.8)	2426	79.4 (77.7-81.2)	3513	87.7 (86.5-89.0)	1771	94.6 (93.5-95.8)	2391	81.6 (79.4-83.9)	1777	68.4 (66.0-70.8)
Unideal	1560	16.4 (15.2-17.5)	903	20.6 (18.8-22.3)	657	12.3 (11.0-13.5)	118	5.4 (4.2-6.5)	543	18.4 (16.1-20.6)	899	31.6 (29.2-34.0)

Abbreviations: CVH, cardiovascular health; BMI, body mass index; BP, blood pressure; TC, total cholesterol; FPG, fasting plasma glucose.

Only 0.15% of the total adults had all 7 ideal CVH metrics and the percentages are low across all the subgroups (**Figures 4.1, 4.2 and 4.3**). 18.72% of participants had 5 to 7 ideal CVH metrics and the proportions varied by sex and age. It was 22.37% for women, 15.12% for men, 36.14% for young adults, 9.20% for middle-aged population, and 3.36% for older adults. 39.85% of participants had 0 to 2 ideal CVH metrics and it also varied by sex and age. It was 34.25% for women, 45.39% for men, 18.24% for young adults, 48.2% for middle-aged population, and 63.94% for older adults. Both males and females most commonly had 2 to 3 ideal components. Young adult subjects most frequently had 4 to 5 ideal metrics, whereas middle-aged and older subjects most frequently had 2 to 3 and 1 to 2 ideal metrics, respectively.

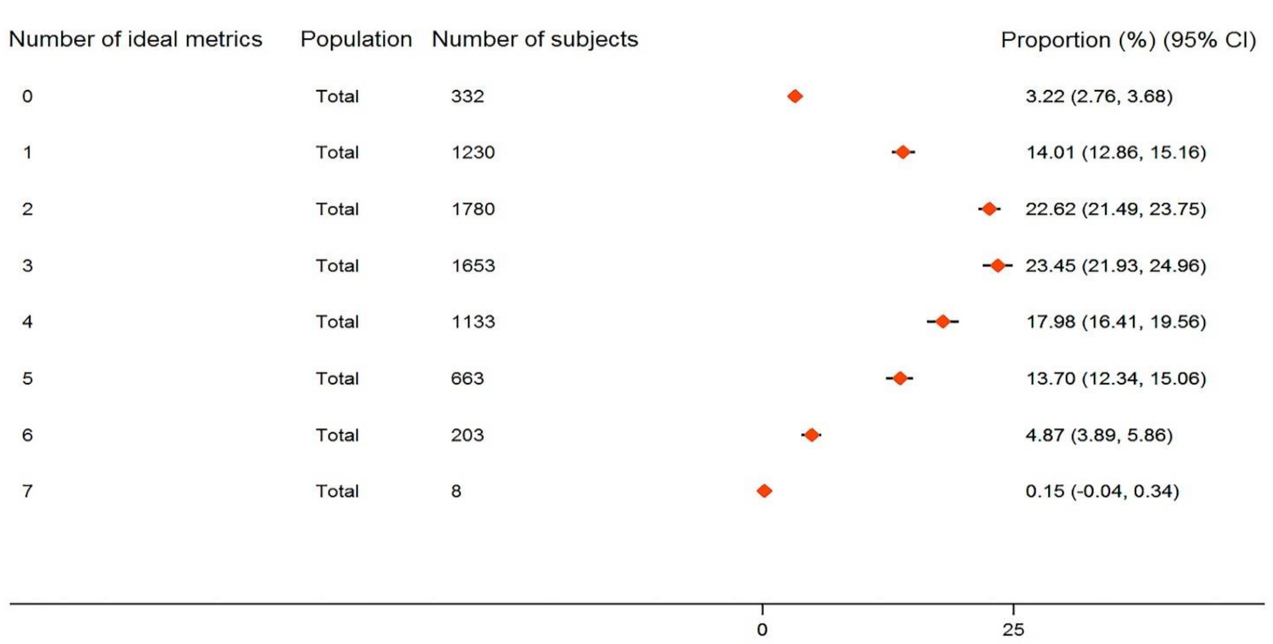

Figure 4.1 Weighted proportions of subjects with different numbers of ideal CVH metrics in the overall population. Error bars indicate 95% CIs. Abbreviations: CI, confidence interval; CVH, cardiovascular health.

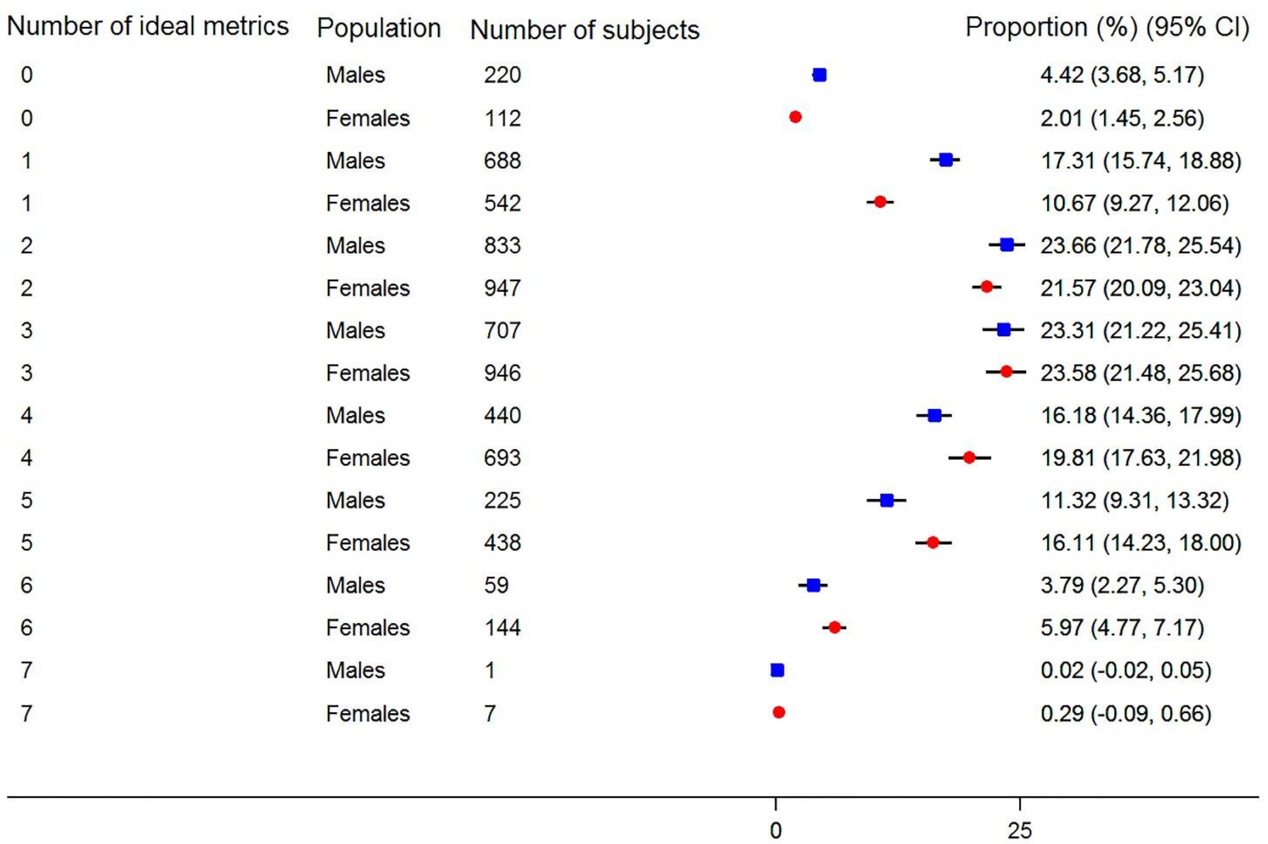

Figure 4.2 Weighted proportions of subjects with different numbers of ideal CVH metrics, stratified by sex. Error bars indicate 95% CIs. Abbreviations: CI, confidence interval; CVH, cardiovascular health.

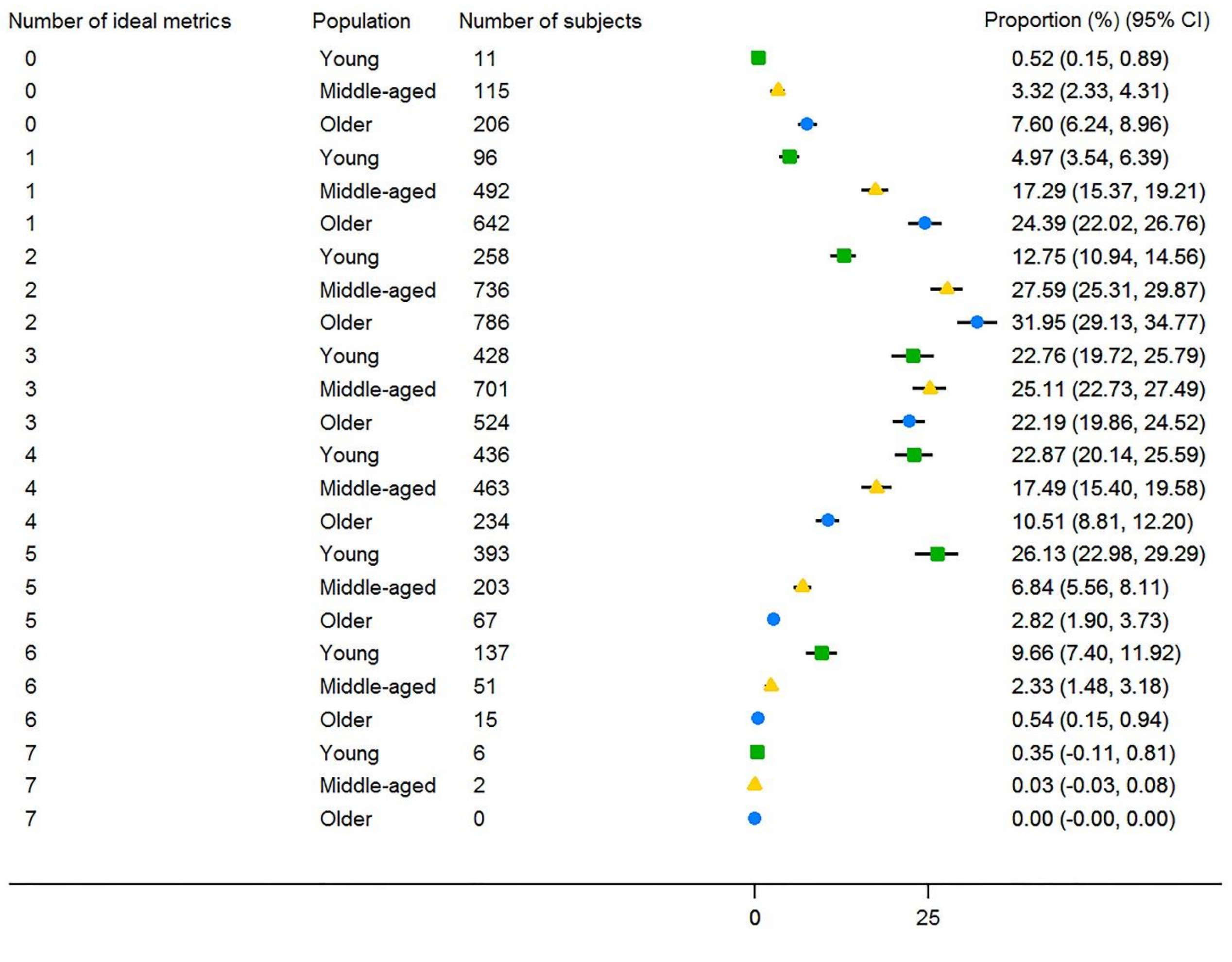

Figure 4.3 Weighted proportions of subjects with different numbers of ideal CVH metrics, stratified by age. Error bars indicate 95% CIs. Abbreviations: CI, confidence interval; CVH, cardiovascular health.

Discussion

To the best of our knowledge, the current study is the first to assess the CVH status, defined by the guidelines of AHA, in Australian adults using a nationally representative sample. There is a substantial difference between the ideal percentages of the seven metrics. Additionally, we observed a very low percentage of the ideal CVH.

Among the seven metrics, FPG (83.6%) and smoking (55.6%) were with the highest proportions of ideal status. In contrast, very few participants have the ideal dietary pattern (4.8%) and physical activity (26.7%) status. Generally, the ranking in our study is consistent with the findings of a systematic review, which summarized the prevalence estimates from ~30 US and non-US studies. [11] The AHA Committee has reported that the estimated ideal percentages of the seven metrics among American adults: smoking status, 73%; BMI, 33%; physical activity, 45%; dietary pattern, < 0.5%; TC, 45%; BP, 42%; and FPG, 58%. [7] In comparison, Australians displayed higher percentages of ideal BMI, dietary pattern and FPG and lower percentages of ideal smoking and physical activity. They have similar proportions of ideal TC and BP.

We estimated that only 0.15% of Australian adults have ideal status on all of the seven metrics, and a number of studies from US, [12, 26, 27, 58] China [55, 80] and Korea [35] also reported the proportion of ideal status for all the seven metrics was below 1%. A large proportion, ~40%, of subjects have ideal status for ≤ 2 metrics, and it is generally consistent with two studies. [12, 27] However, several investigations reported higher [58, 143] or lower [30, 144] rates, indicating the possibilities of regional differences. Given the severe situation, AHA's goal to improve the overall CVH by 20% by 2020 is tricky.

Another interesting phenomenon is the age and sex distinctions in the CVH status. Middle-aged and older adult were more likely to consume sufficient fruits and vegetables when compared to younger adults. A possible explanation is participants in those two groups were tend to have higher income, which was positively associated with fruits' and vegetables' consumption. [165] Younger adults demonstrated better status in other six metrics as well as the overall CVH status. Thus, it is urgent to promote the CVH status in middle- and older-aged individuals as adhering and maintaining a healthy lifestyle has dramatic effects on CVD risk reduction among those age groups. [137, 166] Females tend to take fewer physical activities than males do, and a relatively longer duration of TV viewing time among women may be partly responsible for the sex difference. [167] We observed larger proportions of ideal status for the other metrics, as well as greater number of ideal overall CVH status, among females when compared to males. Given the situation, the policy makers should pay more attention to the alarming CVH status of Australian males in order to close the sex gap.

To our delight, some Australian research institutions have also recognized the significance of CVD prevention. The National Vascular Disease Prevention Alliance has updated the guidelines for the management of absolute CVD risk in 2012 and extended the age range, from 45 to 74 years to 45 years or older, of eligible participants for CVD risk assessment. [10] The Australian Diabetes, Obesity and Lifestyle Study has explored the relationships between several risk factors, like longer television viewing time [167] and diabetes, [168] with CVD mortality in a large national cohort. Our findings have extended their efforts by including all adults, aged 18 years or older, and analysing the combined effects of multiple CVD contributors. Given the fact that only a small proportion of subjects, < 40% for all age and sex subgroups, were with 5-7 ideal CVH metrics, the population-wide strategy should be promoted to shift the entire distribution of CVD risk. The low prevalence of ideal dietary pattern and physical activity suggests that we should put in more efforts to improve the status of these two metrics. Public awareness of CVD modifiable factors, promotion of laws and regulations to restrict unhealthy food, as well as improvement of access to fitness facilities could be effective measures to enhance the overall CVH status among Australian adults.

Several limitations of the current study should be considered. First, although our study was based on a nationally representative sample and used biomedical sampling weight, it may still have the risk of selection bias, as there are some differences for some demographic factors and CVH metrics between participants and non-participants (**Table 4.2**). Second, the current study was a cross-sectional study and, thus, we cannot explore the temporal trend of the CVH status as well as Life's Simple 7 and future CVD risk. Third, we were unable to take some other CVD influencing factors, such as menopause, into consideration due to limited variables and sample size. Fourth, our study only used one recall to measure dietary intake. Finally, we modified the AHA's definition of CVH due to the data structures, and it may lead to some misclassifications. For instance, we only used fruits and vegetables to measure dietary pattern, as other dietary components defined by the AHA were not existed in our survey.

Conclusion

Our study demonstrates that the prevalence of the ideal CVH is very low amongst Australian adults. The ideal status is less prevalent for some metrics, such as the dietary pattern and physical activity. Public health policies should be implemented to promote the overall CVH status.

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Disclosure

The authors report no conflicts of interest in this work.

Chapter 5 – The CVH status and CVD prevalence in Australian adults

Chapter 3 has summarized the findings on the associations between the CVH status the CVD risk. The separate effects of the CVH metrics on CVD risk are limited and inconsistent and the strength of association between the ideal CVH number and CVD risk varied by studies. Therefore, we illustrated the separate and combined associations between the CVH status and CVD prevalence in overall Australian adults using the core sample of the 2011-2012 AHS (Chapter 5.1). The sex and age variations in the magnitude of association were also explored (Chapter 5.2). This chapter addressed the research objective 4 of the thesis.

5.1 The CVH status and CVD prevalence in the overall Australian adults

This section was formatted as the following publication:

Peng Y, Wang Z. *Association of Life's Simple 7 and presence of cardiovascular disease in general Australians*. Open Heart 2017; 4(2): e000622. doi: 10.1136/openhrt-2017-000622.

Contributor	Statement of contribution
Yang Peng (Candidate)	Conception and design (70%) Data analysis and result interpretation (100%) Drafting of article (100%) Reviewing of article (50%)
Zhiqiang Wang	Conception and design (30%) Reviewing of article (50%)

Association of Life's Simple 7 and presence of cardiovascular disease in general Australians

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ABSTRACT

Objective: The AHA developed Life's Simple 7 to define and monitor the CVH, but their associations and contributions to CVD prevalence in general Australians are still unclear. Our study is to evaluate the separate and combined associations and contributions of Life's Simple 7 and self-reported CVD prevalence among Australians.

Methods: We performed a cross-sectional study based on 7499 adults (≥18 years) who have tested for TC and FPG as part of the 2011-2012 AHS. The self-reported CVD prevalence was the outcome of our study, and it was based on the 10th version of International Classification of Diseases, codes I00-I99. Poisson regression analyses were used to estimate the incidence rate ratios (IRRs) and population attributable fractions (PAFs) of those metrics to CVD prevalence. Participants were classified into three CVH status groups based on the number of ideal metrics: poor (0-2), intermediate (3-4), and ideal (5-7). Logistic regression analyses were performed to illustrate the relationships between the overall CVH and CVD prevalence.

Results: Two thousand one hundred (21.0%) participants had CVD. Smoking, elevated BMI, BP, TC, FPG, and physical inactivity were observed as significant indicators of CVD prevalence. Compared to the inadequate category, participants in the optimal and average category have a 66% [adjusted OR, 0.34; 95% CI, 0.22-0.54] and a 33% (adjusted OR, 0.67; 95% CI, 0.56-0.81) lower CVD prevalence. One more ideal metric was associated with a 21% reduced CVD prevalence (adjusted OR, 0.79; 95% CI, 0.73-0.84).

Conclusions: We have identified several modifiable risk factors and contributors of CVD prevalence in general Australians. The improvement of the overall CVH may also reduce CVD prevalence.

KEY QUESTIONS

What is already known about this subject?

Life's Simple 7 is associated with the CVD prevalence in US and some other regions. The magnitudes of individual and/or combined associations of Life's Simple 7 varied across studies.

What might this study add?

Most factors of the Life's Simple 7 and the overall CVH were significantly related to CVD prevalence in general Australians.

How might this impact on secondary prevention of CVD?

Life's Simple 7 is an easily implementable tool in secondary prevention of CVD. Hence, doctors and other professionals can provide CVD prevention tips to CVD patients based on their Life's Simple 7 status.

Introduction

CVD is still a leading cause of mortality and, in 2013, it contributed to over 0.8 million deaths in the USA. [169] According to the Global Burden of Disease Study, CVD accounted for more than 30% global overall deaths in 2013. [19] In Australia, CVD is also one of the major contributors to mortality. IHD, the most common type of CVD, ranked as the first cause of mortality among Australians. [170]

To define and monitor the CVH in general Americans, the AHA released 7 modifiable cardiovascular behaviors [including smoking status, BMI, physical activity and dietary pattern] and factors [including smoking status (also treated as a behavior), TC, BP and FPG] and they are also called Life's Simple 7. [7] To date, a number of studies have examined the individual and combined effects of Life's Simple 7 on CVD risk. Several cohort studies have observed the significant graded relationship between the number of ideal CVH metrics and CVD incidence [143, 160] and CVD mortality. [35, 146] It is also reported that the ideal status of most CVH metrics were significantly associated with reduction of CVD mortality. [35, 146] However, few studies have explored the association between Life's Simple 7 and CVD risk in Australian adults.

The present study used an Australian representative sample collected from the 2011-2012 AHS, aiming to clarify the individual and combined associations between Life's Simple 7 and CVD prevalence. We hypothesized that there is a negative association between number of ideal CVH metrics and CVD prevalence in Australian adults, and most metrics were significantly associated with CVD prevalence.

Methods

Study design and subjects

We retrospectively analyzed data from the core sample of the 2011-2012 AHS, a national wide and population-based combined sample of three surveys: NHS, NNPAS, and NHMS, which included participants from the first two surveys who provided biomedical samples. ABS organized the three surveys. NHS and NNPAS used a stratified multistage random sample from private dwellings usual residents in urban and rural areas of all states in Australia, covering about 97% of the people living in Australia. Overseas visitors staying or intending to stay in Australia for 12 months or more are in scope. Households in Very Remote areas of Australia and discrete Aboriginal and Torres Strait Islander communities were excluded. Trained interviewers obtained the NHS and NNPAS information through face-to-face Computer Assisted Personal Interview. For the 24-hour dietary recall collection, Computer Assisted Telephone Interview was used. All participants aged 12 or over and aged 5 or over in both NHS and NNPAS were asked to voluntarily provide fasting blood samples and urine samples, which constituted the NHMS, to the convenient collection centers and Sonic Healthcare processed the samples. The current NHS was the sixth in a series of regular population surveys and previous ones were conducted in 1989-90, 1995, 2001, 2004-05 and 2007-08. NNPAS and NHMS were new surveys. NHS, NNPAS and NHMS were enumerated from 6 March 2011 to 17 March 2012, 29 May 2011 to 9 June 2012 and March 2011 to September 2012, respectively. The core sample consisted of 24910 adults (≥ 18 years old) and age was determined by the NHS or NNPAS interview date. We restricted our study to those who voluntarily participated in both TC and FPG tests (n=7499), yielding an overall response rate of 30.1%. All participants provided written informed consent and our study was approved by The School of Medicine Low Risk Ethical Review Committee in the University of Queensland (approval number 2016-SOMILRE-0161).

Life's Simple 7

All modifiable metrics were divided into ideal and non-ideal status. The detailed classification criteria were shown in **Table 5.1**. Based on the number of ideal metrics, participants were grouped into 3 CVH categories: poor (0-2), intermediate (3-4) and ideal (5-7). [171]

Table 5.1 Definition of Life's Simple 7 ideal and unideal status in our study.

Factors	Ideal	Non-ideal
Smoking	Never smokers	Current and former smokers
BMI	< 25 kg/m^2	≥ 25 kg/m^2
Physical activity*	≥ 150 min/week moderate or ≥ 75 min/week vigorous or ≥ 150 min/week moderate + vigorous	< 150 min/week moderate, < 75 min/week vigorous and < 150 min/week moderate + vigorous
Dietary pattern#	Having met the fruits and vegetables intake requirement defined by 2013 Australian Dietary Guidelines	Having not met the fruits and vegetables intake requirement defined by 2013 Australian Dietary Guidelines
TC	TC < 200 mg/dL and not taking cholesterol-lowing medication	TC ≥ 200 mg/dL and/or taking cholesterol-lowing medication
BP	Systolic BP < 120 mm Hg and diastolic BP < 80 mm Hg	Systolic BP ≥ 120 mm Hg and/or diastolic BP ≥ 80 mm Hg
FPG	< 100 mg/dL	≥ 100 mg/dL

Abbreviations: BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

* Moderate physical activity refers to any exercise that caused a moderate increase in heart rate or breathing (e.g. gentle swimming, social tennis, golf). Vigorous physical activity refers to any exercise that caused a large increase in heart rate or breathing (e.g. jogging, cycling, aerobics, competitive tennis).

The 2013 Australian Dietary Guidelines recommended at least 2 serves of fruits for all adults, 5 serves of vegetables for males aged over 70 and all females, 5.5 serves of vegetables for males aged between 51 and 70 and 6 serves of vegetables for males aged 50 or younger.

Outcome measurement

The self-reported CVD prevalence was based on the 10th version of International Classification of Diseases (ICD), codes I00-I99. To be more specific, our study treated angina, stroke, rheumatic heart disease, heart attack, HF, hypertension, hypotension, hardening of the arteries/atherosclerosis/arteriosclerosis, varicose veins, rapid or irregular heartbeats/tachycardia/palpitations and any other participant self-entered I00-I99 conditions as CVD. Respondents were asked whether a doctor or a nurse has ever told them that they have those conditions, respectively. They were asked whether they currently have the condition if they have chosen yes to any of them. Those who have been told and currently have at least one of the above conditions were regarded as positive for CVD prevalence in our study.

Covariates

The following variables were adjusted as covariates in the present study: age (continuous), sex, education attainment, income status, and residence region. Education attainment was categorized as high (≥ 12 school years) and low (< 12 school years). Income status was evaluated by household income and dichotomized as low (≤ 50th percentile equivalised weekly household income) and high (> 50th percentile equivalised weekly household income). Residence region was classified into major cities, inner regional areas and other areas (outer regional and remote areas).

Statistical analysis

Firstly, we used univariate and multivariate Poisson regression analysis to calculate crude (unadjusted) and adjusted IRRs and corresponding 95% CIs and, thus, to elucidate the association between preventable factors and CVD prevalence.

Secondly, we calculated the adjusted PAFs based on the following equation to measure the effects of each component on CVD reduction. [172] Pe is the prevalence of exposure and Rate Ratios (RRs) were replaced with adjusted IRRs.

$$PAF = \frac{Pe \times (RR - 1)}{1 + Pe \times (RR - 1)}$$

Thirdly, we calculated ORs using logistic regression analyses to explore the relationship between the overall CVH and CVD prevalence. Participants with missing values in one or more of Life’s Simple 7 components were not included in the analyses.

To infer results for the total in-scope population, we used biomedical weight and Jackknife method in the Life’s Simple 7 and CVD association analyses. All analyses were conducted within the ABS's RADL with Stata version 10.0. A two-sided *P* value < 0.05 was used to determine statistical significance.

Results

For the 7499 participants, 2100 are positive for CVD, with a weighted prevalence of 21.0%. Among the 7 metrics, FPG has the highest weighted ideal proportion (83.6%), followed by smoking status (55.6%), TC (45.5%), BP (44.2%), BMI (39.2%), physical activity (26.7%), and dietary pattern (4.8%). The metrics and covariates details of the participants are summarized in **Table 5.2**.

Table 5.2 Characteristics of Life's Simple 7 and covariates in the current study.

Variables	Status	With CVD		Without CVD		Overall	
		n/N	%*	n/N	%*	n/N	%*
Smoking	Ideal	947/2100	47.2	2815/5399	57.8	3762/7499	55.6
	Unideal	1153/2100	52.8	2584/5399	42.2	3737/7499	44.4
BMI	Ideal	462/1977	25.2	1933/5150	42.9	2395/7127	39.2
	Unideal	1515/1977	74.8	3217/5150	57.1	4732/7127	60.8
Physical activity	Ideal	326/2099	16.0	1448/5396	29.6	1774/7495	26.7
	Unideal	1773/2099	84.0	3948/5396	70.4	5721/7495	73.3
Dietary pattern	Ideal	141/2100	5.4	293/5399	4.6	434/7499	4.8
	Unideal	1959/2100	94.7	5106/5399	95.4	7065/7499	95.2
TC	Ideal	506/2100	28.0	2321/5399	50.1	2827/7499	45.5
	Unideal	1594/2100	72.0	3078/5399	49.9	4672/7499	54.5
BP	Ideal	523/2019	25.8	2305/5202	49.1	2828/7221	44.2
	Unideal	1496/2019	74.2	2897/5202	50.9	4393/7221	55.8
FPG	Ideal	1376/2100	68.8	4563/5399	87.6	5939/7499	83.6
	Unideal	724/2100	31.2	836/5399	12.4	1560/7499	16.4
Age	< 60 years	753/2100	40.8	4070/5399	84.7	4823/7499	75.5
	≥ 60 years	1347/2100	59.3	1329/5399	15.3	2676/7499	24.5
Sex	Male	952/2100	47.1	2377/5399	49.9	3329/7499	49.3
	Female	1148/2100	52.9	3022/5399	50.1	4170/7499	50.7
Education level	High	682/2100	35.7	3051/5399	63.7	3733/7499	57.9
	Low	1418/2100	64.3	2348/5399	36.3	3766/7499	42.1
Income	High	674/1918	36.1	2726/4899	57.9	3400/6817	53.2
	Low	1244/1918	63.9	2173/4899	42.1	3417/6817	46.8
Region	Major cities	1184/2100	66.7	3378/5399	74.0	4562/7499	72.5
	Inner regional	553/2100	23.1	1156/5399	18.7	1709/7499	19.6
	Other	363/2100	10.1	865/5399	7.3	1228/7499	7.9

Abbreviations: BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CVD, cardiovascular disease.
* Weighted prevalence using biomedical weight.

In the univariate analysis, all of the factors, except for dietary pattern, are positively associated with CVD prevalence. The relationships still exist after adjusted for covariates. High BMI (adjusted IRR: 1.37; 95% CI: 1.21-1.55, *P*<0.01), elevated FPG (adjusted IRR: 1.34; 1.21-1.49, *P*<0.01), elevated BP (adjusted IRR: 1.27; 1.10-1.47, *P*<0.01), physical inactivity (adjusted IRR: 1.23; 1.00-1.52, *P*=0.049), elevated TC (adjusted IRR: 1.21; 1.06-1.38, *P*=0.01) and smoking (adjusted IRR: 1.18; 1.04-1.34, *P*=0.01) are significantly associated with higher CVD prevalence (**Table 5.3**). We calculated adjusted PAFs to quantify the contributions of certain factors to CVD prevalence (**Figure 5.1**). High BMI is the largest significant contributor to CVD prevalence, with adjusted PAF of 20%, followed by physical inactivity (15%), elevated BP (14%), elevated TC (12%), smoking (8%) and elevated FPG (7%).

Table 5.4 displays the relationship between the number of ideal metrics and CVD prevalence. Compared to those in the poor category, those in the ideal category had a reduction of 66% in CVD prevalence (adjusted OR: 0.34; 95% CI: 0.22-0.54) and those in the intermediate category had a reduction of 33% in CVD prevalence (adjusted OR: 0.67; 95% CI: 0.56-0.81). On average, one more ideal metric was associated with a 21% reduced risk of CVD prevalence (adjusted OR: 0.79; 95% CI: 0.73-0.84).

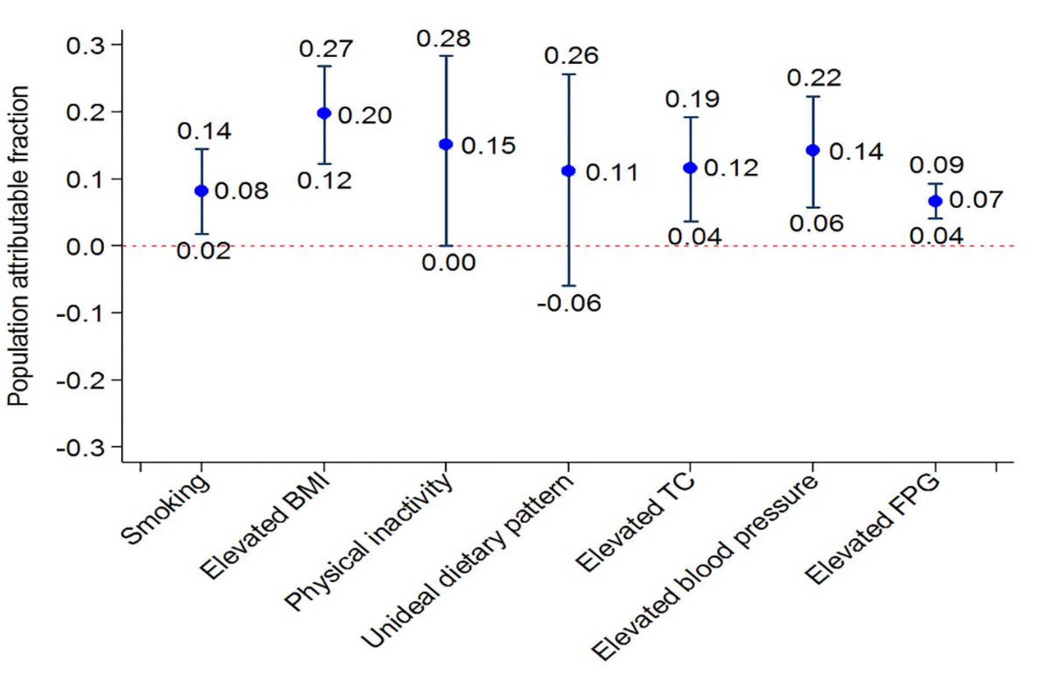

Figure 5.1 Adjusted PAFs of the CVH metrics to CVD prevalence in the overall population. Abbreviations: TC, total cholesterol; FPG, fasting plasma glucose; CVH, cardiovascular health; CVD, cardiovascular disease.

Table 5.3 IRRs between the individual CVH metrics and CVD prevalence in the overall population.

Variables	Crude IRR (95% CI)	*P*	Adjusted* IRR (95% CI)	*P*
Smoking	1.40 (1.24-1.58)	< 0.01	1.18 (1.04-1.34)	0.01
Elevated BMI	1.92 (1.64-2.24)	< 0.01	1.37 (1.21-1.55)	< 0.01
Physical inactivity	1.91 (1.59-2.30)	< 0.01	1.23 (1.00-1.52)	0.049
Unideal dietary pattern	0.88 (0.69-1.12)	0.29	1.13 (0.94-1.37)	0.19
Elevated TC	2.14 (1.88-2.44)	< 0.01	1.21 (1.06-1.38)	0.01
Elevated BP	2.28 (1.96-2.66)	< 0.01	1.27 (1.10-1.47)	< 0.01
Elevated FPG	2.32 (2.09-2.57)	< 0.01	1.34 (1.21-1.49)	< 0.01

Abbreviations: IRR, incidence rate ratio; CVH, cardiovascular health; CVD, cardiovascular disease; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CI, confidence interval.

* Adjusted for age (continuous), sex, education attainment, income, and residence region.

Table 5.4 ORs between the number of ideal metrics and CVD prevalence in the overall population.

Ideal metrics number	CVD cases/participants	Crude OR (95% CI)	*P*	Adjusted* OR (95% CI)	*P*
0-2	1283/3342	Referent	--	Referent	--
3-4	585/2786	0.41 (0.35-0.48)	< 0.01	0.67 (0.56-0.81)	< 0.01
5-7	70/874	0.09 (0.06-0.14)	< 0.01	0.34 (0.22-0.54)	< 0.01
One more ideal metric	--	0.60 (0.57-0.63)	< 0.01	0.79 (0.73-0.84)	< 0.01

Abbreviations: OR, odds ratio; CVD, cardiovascular disease; CI, confidence interval.

* Adjusted for age (continuous), sex, education attainment, income, and residence region.

Discussion

To the best of our knowledge, it is the first study that explored the individual and combined effects of Life's Simple 7 on CVD prevalence among general non-indigenous Australians. We observed that raised BMI, physical inactivity, increased BP, unideal TC, smoking and elevated FPG are independent risk factors and contributors of CVD. Higher number of ideal metrics is associated with reduced CVD prevalence.

High BMI was the largest contributor to CVD prevalence in our study. Several previous reports also identified overweight/obesity as a significant risk factor of CVD. [42, 173, 174] Moreover, it has reported that the prevalence of obese is still increasing over time. In Australia, the age-standardized obesity prevalence has more than doubled from 1980 to 2000. [175] Similar increased trends in overweight and/or obesity were also observed in adults from China, [176] USA, [177] Mongolia [178] and Polish. [179] Additionally, we noticed that unideal status of physical activity, BP, TC, smoking and FPG are also significant contributors to CVD prevalence in our study. Their roles in elevating the CVD risks were also been confirmed in a number of studies, [146, 174, 180, 181] which suggested the relevant intervention programs are needed to improve the CVH.

Similar to our findings, two US studies also identified BMI as the most crucial contributor to coronary artery calcification [182], and VTE, [63] respectively, while a number of studies from USA, [30, 36, 144, 171] China [42, 146, 174] and Korea [35] ranked unideal BP as the most significant contributor of CVD mortality, [30, 35, 144, 146, 171] CVD incidence [174] and stroke incidence. [36, 42] The inconsistency in rankings may suggestive of various risk factor patterns of different diseases and populations.

Dietary pattern was not independently related to CVD reduction in the current study. Several studies have identified dietary pattern [174, 183, 184] as a CVD risk factors. However, some studies failed to reveal the association. [35, 36] A possible explanation of the conflicting findings may due to the various definitions of dietary pattern status in each study. Thus, more studies are warrant to test the relationship more accurately.

We have observed that CVD prevalence showed declining trends with increasing number of the ideal CVH metrics, behaviors and factors. Our findings are consistent with several studies, which also found the graded inverse relationship between favorable ideal metrics and CVD mortality [143, 144, 146, 171] and incidence. [12, 36, 63, 180] Our results, along with those of previous studies, suggested that those factors may interrelate with each other and a small improvement of the CVH might have a dramatic reduction of CVD burden.

There are some limitations to our study. First, it is a cross-sectional study and we are unable to examine temporality between Life's Simple 7 and CVD incidence or mortality. More cohort studies are needed to explore the causal relationship between Life's Simple 7 and CVD incidence and mortality. Second, we used modified metrics definitions owing to the AHS dataset structures. For example, the AHA guideline included five components for dietary pattern. However, our study only included fruits and vegetables as other components were not available in our survey. Third, the CVD prevalence was self-reported, and it may not be completely accurate. Previous studies observed that, when compared between self-reported questionnaire and medical record data, there are fair to substantial agreement for MI [185-187] and stroke. [185, 186] Fourth, as most of the CVD types in our study were coded as other CVDs, we are unable to provide detailed prevalence and risk factors for certain types of CVDs. Fifth, the sample excluded those living in the very remote areas and indigenous communities, though their population proportion is very small. Although our findings are representative of the target population by using the biomedical weight, we may still have the risk of selection bias because there are some differences in demographic characteristics and CVH metrics between participants and non-participants (**Table 4.2**). Sixth, since the log-binomial regression was not allowed in the ABS system, the usage of logistic/poisson regression may overestimate the association between the number of ideal CVH metrics and CVD prevalence.

In summary, we identified BMI, increased BP, physical inactivity, unideal TC, smoking and elevated FPG as significant risk factors and contributors of CVD prevalence in the general Australians. The higher number of ideal Life's Simple 7 metrics was associated with reduced risk of CVD.

Contributors YP and ZW: concept/design; YP: data analysis/interpretation; YP: drafting article; ZW: critical revision of article; YP and ZW: approval of article.

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Competing interests None declared.

Ethics approval The School of Medicine Low Risk Ethical Review Committee in the University of Queensland.

5.2 The CVH status and CVD prevalence in the Australian sex and age subgroups

This chapter was based on a paper submitted:

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Contributor	Statement of contribution
Yang Peng (Candidate)	Conception and design (70%) Data analysis and result interpretation (100%) Drafting of article (100%) Reviewing of article (50%)
Zhiqiang Wang	Conception and design (30%) Reviewing of article (50%)

Sex and age disparities in the association between cardiovascular health metrics and self-reported cardiovascular disease prevalence in Australian adults

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Abstract

Background: The AHA outlined seven CVH metrics to define and monitor the CVH status. Our study aimed to evaluate the sex and age disparities in the association between these metrics and CVD prevalence using a nationally representative survey.

Methods: We included 7499 adults (≥ 18 years) from the core sample of the 2011-2012 AHS. The exposures included seven CVH metrics and overall CVH status, defined by the number of ideal metrics. The outcome was the self-reported CVD prevalence. We calculated the IRRs and ORs to measure the associations between individual CVH metric/ the ideal metrics number and CVD prevalence in each sex and age subgroup and entered the interaction terms to compare the strengths of associations between subgroups. In addition, we obtained the PAFs to measure the contributions of CVH metrics to CVD prevalence in each age/sex subgroup.

Results: The associations and contributions of elevated TC and BP to CVD prevalence were stronger in males than in males. Physical inactivity and unhealthy dietary pattern have stronger impacts on CVD prevalence in older and young adults, respectively. The association between ideal metrics number and CVD prevalence was more pronounced among males compared to females.

Conclusion: We observed the sex and age variations in the magnitude of associations between CVH metrics and CVD prevalence. The findings need further explorations in large-scale prospective studies.

Keywords: cardiovascular health, cardiovascular disease; sex; age

KEY QUESTIONS

What is already known about this subject?

► The CVH metrics were associated with CVD risk.

► Little was known about the sex and age variations in the magnitude of the association.

What does this study add?

► Elevated BP, elevated TC, and the number of ideal metrics have greater impacts on CVD prevalence in males than females.

► Physical inactivity has a stronger association with CVD prevalence in older adults.

► The association between unhealthy dietary pattern and CVD prevalence was more obvious in young adults.

How might this impact on clinical practice?

► Sex and age-specific strategies should be developed and implemented to improve the CVH status.

Introduction

CVD is still one of the major contributors to health burden globally. CVD has contributed to over 17.6 million deaths, almost one-third of all deaths, globally in 2016. [1] Previous studies suggested that a healthy lifestyle factors played a central role in the prevention of CVD. [5, 6] A study of The China Kadoorie Biobank reported that 67.9% of major coronary events were attributable to poor status of six lifestyle factors. [5] Similarly, a US study revealed that non-ideal status of six lifestyle-related metrics was associated with more than 70% of CHD cases. [6]

In this context, the AHA established the concept of CVH status. In addition, the AHA identified seven lifestyle-related behaviors and factors (smoking status, BMI, physical activity, healthy diet, TC level, BP level, and FPG level) to measure CVH status in the general subjects. [7] A number of studies reported that these metrics were significantly associated with CVD risk reduction. [91, 149, 151] A European cohort observed the significant association between CVH status and incidence of CVD, CHD, and stroke. [149] A cohort study in US found the negative association between the number of CVH metrics and HF incidence. [91] An Australian cross-sectional study noticed the CVH metrics correlated to the CVD prevalence. [151] However, very few studies have focused on the impacts sex/age on the association strengths between CVH metrics and CVD risk. Identification of sex and age variances in the relationships between CVH metrics and CVD risk is crucial for prioritizing preventive strategies in sex and age subpopulations.

Our study aimed to elucidate the individual and combined associations between the CVH metrics and CVD prevalence in sex and age-specific populations. We hypothesized that the CVH metrics have greater impacts on CVD prevalence among males and older adults. We used a nationally representative sample, the core sample of the 2011-2012 AHS, to conduct our analyses.

Methods

Study design and participants

Details of the study design and participants have been described previously. [151, 188] Briefly, our study used the core sample of the 2011-2012 AHS, a nationwide and population-based combined sample of three surveys: National Health Survey (NHS), National Nutrition and Physical Activity Survey (NNPAS), and National Health Measures Survey (NHMS), which included participants from the first two surveys who provided biomedical samples. NHS and NNPAS used a stratified multistage random sample from private dwellings usual residents in urban and rural areas of Australia. Overseas visitors staying or intending to stay in Australia for 12 months or more are in scope. Households in very remote areas and discrete Aboriginal and Torres Strait Islander communities were excluded. Trained interviewers obtained the 24-hour dietary recall collection via computer-assisted telephone interview and other NHS and NNPAS information via face-to-face, computer-assisted personal interview. All participants aged 12 or over and 5 or over in both NHS and NNPAS were asked to voluntarily provide fasting blood samples and urine samples, which constituted the NHMS, to the convenient collection centres. As a number of participants have no information on TC and FPG, we restricted to adults (≥ 18 years) with available data of TC and FPG tests, yielding to an overall sample size of 7499 and a response rate of 30.1%. According to the guideline of the survey, the analyses on the included subjects could be nationally representative of the health status of general Australians using the biomedical weight. A small proportion of participants have missing data on other metrics, and the group Jackknife weights could correct the possible non-response bias. The sample sizes for the associations between individual metrics and CVD prevalence ranged from 7127 to 7499. A total of 7002 participants have no missing data on all seven metrics, and they were included in the analyses between overall CVH status and CVD prevalence. Participants were classified into young (18-39 years), middle-aged (40-59 years), and older (≥ 60 years) adults based on the age while taking the survey. All participants provided written informed consent, and our study was approved by The University of Queensland Medicine, Low & Negligible Risk Ethics Sub-Committee (approval number 2018000244).

CVH metrics

We divided all CVH metrics into ideal and non-ideal status (**Table 5.5**). [151, 188] We modified the definitions of ideal smoking, dietary pattern, BP and FPG due to the lack of information on the time since quit smoking, several dietary components, and medications on BP and FPG in our survey. On the interview date, information on smoking, physical activity, and cholesterol-lowering medication was collected through questionnaires. BMI and BP were measured by digital scales and automated BP monitor, respectively. The 24-hour dietary recall determined the dietary pattern. Blood samples were used for TC and FPG measurements, and they were measured by Cholesterol Oxidase assay and Hexokinase assay, respectively. Participants having 0-2, 3-4, and 5-7 ideal metrics were referred to as being in overall poor, intermediate, and ideal CVH status. [84]

Table 5.5 Classifications of the seven CVH metrics in our study.

Metrics	**Ideal**	**Non-ideal**
Smoking	Never smokers	Current and former smokers
BMI	< 25 kg/m^2	≥ 25 kg/m^2
Physical activity	≥ 150 min/week moderate or ≥ 75 min/week vigorous or ≥ 150 min/week moderate + vigorous	< 150 min/week moderate, < 75 min/week vigorous and < 150 min/week moderate + vigorous
Dietary pattern	Having met the fruits and vegetables intake requirement defined by 2013 Australian Dietary Guidelines	Having not met the fruits and vegetables intake requirement defined by 2013 Australian Dietary Guidelines
TC	< 200 mg/dL and not taking cholesterol-lowering medicine	≥ 200 mg/dL and/or taking cholesterol-lowering medicine
BP	Systolic BP < 120 mm Hg and diastolic BP < 80 mm Hg	Systolic BP ≥ 120 mm Hg and/or diastolic BP ≥ 80 mm Hg
FPG	< 100 mg/dL	≥ 100 mg/dL

Abbreviations: CVH, cardiovascular health; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

Outcome measurement

The CVD prevalence was self-reported and based on the 10th version of International Classification of Diseases, codes I00-I99. To be more specific, participants were regarded as having a CVD condition if they had been told by a doctor or nurse that they had CVD and they currently have CVD while taking the survey.

Covariates

The following variables were adjusted as they previously are shown to relate to CVD risk [189, 190] and their information was available in our study: age (continuous), sex, education attainment, income status, and residence region. Education attainment was categorized as high (≥ 12 school years) and low (< 12 school years). Income status was evaluated by household income and dichotomized as low (≤ 50th percentile equivalised weekly household income) and high (> 50th percentile equivalised weekly household income). Residence region was classified into major cities, inner regional areas and other areas (outer regional and remote).

Statistical analysis

Firstly, we compared CVD prevalence, ideal metrics, and covariates between sex and age groups using weighted chi-square tests.

Secondly, we explored the possible sex and age variations in the associations and contributions of individual metrics and CVD prevalence. We calculated IRRs and corresponding 95% CIs, using univariate and multivariate Poisson regression analysis, to elucidate the association between CVH metrics and CVD prevalence in each sex- and age-specific group. Interaction terms between sex/age and metrics were included in the adjusted models to explore the potential sex/age differences in the association.

Additionally, we calculated adjusted PAFs and corresponding 95% CIs, for each sex and age group, based on the following equation to measure the impact of each metric on CVD prevalence reduction. *Pe* is the prevalence of non-ideal metric and RRs were replaced with adjusted IRRs.

$$PAF = \frac{Pe \times (RR - 1)}{1 + Pe \times (RR - 1)}$$

Thirdly, we calculated ORs and corresponding 95% CIs using logistic regression analyses to explore the relationship between overall CVH status, defined by the number of ideal metrics, and CVD prevalence in sex and age subgroups. Interaction terms between sex/age and the CVH categories/the ideal metrics number were included in the adjusted models. Participants with missing values in one or more of CVH metrics were not included in the analyses.

To infer results for the in-scope population, we used biomedical weight, and group Jackknife method with 60 replicate weights in the analyses. All analyses were conducted within the ABS's RADL with Stata 10.0. A two-sided P value < 0.05 was used to determine statistical significance.

Results

Baseline characteristics

The baseline characteristics of the included participants were listed in **Table 5.6**. Overall, weighted 21.0% participants were positive for CVD prevalence (2100/7499). Males and females have similar CVD prevalence (20.0% versus 21.9%, P = 0.051) whereas there is a raising CVD prevalence with the increase of age (4.0% for young adults, 19.7% for middle-aged adults, and 50.6% for older adults, P < 0.01). Females have markedly higher rates of ideal smoking, BMI, dietary pattern, BP, and FPG while having a lower rate of ideal physical activity compared with males. Females have higher proportions of middle-aged/older adults and lower income. There is no statistical differences regarding education status, residential region distribution, and ideal TC in both sexes. With the increase of age, there is a significantly higher prevalence of ideal dietary pattern and lower prevalence of ideal status for the other six metrics. Older adults tend to have a lower proportion of males, lower income, and lower education level and less likely to reside in major cities as compared to middle-aged and young counterparts.

Table 5.6 Baseline characteristics of the included participants.

Metrics	Status	Males, n (%)	Females, n (%)	*P*	Young, n (%)	Middle-aged, n (%)	Older, n (%)	*P*
CVD	Yes	952 (20.0)	1148 (21.9)	0.051	104 (4.0)	649 (19.7)	1347 (50.6)	< 0.01
	No	2377 (80.0)	3022 (78.1)		1785 (96.0)	2285 (80.3)	1329 (49.4)	
Smoking	Ideal	1420 (49.8)	2342 (61.1)	< 0.01	1146 (64.8)	1375 (49.5)	1241 (49.0)	< 0.01
	Non-ideal	1909 (50.2)	1828 (38.9)		743 (35.2)	1559 (50.5)	1435 (51.0)	
BMI	Ideal	833 (32.3)	1562 (46.2)	< 0.01	873 (53.7)	877 (30.9)	645 (27.2)	< 0.01
	Non-ideal	2388 (67.7)	2344 (53.8)		916 (46.3)	1927 (69.1)	1889 (72.8)	
Physical	Ideal	945 (32.7)	829 (20.9)	< 0.01	630 (35.4)	690 (23.9)	454 (16.6)	< 0.01
	Non-ideal	2382 (67.3)	3339 (79.1)		1257 (64.6)	2243 (76.1)	2221 (83.4)	
Dietary pattern	Ideal	93 (2.1)	341 (7.4)	< 0.01	73 (3.7)	150 (4.5)	211 (6.9)	< 0.01
	Non-ideal	3236 (97.9)	3829 (92.6)		1816 (96.3)	2784 (95.5)	2465 (93.1)	
TC	Ideal	1259 (45.1)	1568 (45.8)	0.70	1210 (66.8)	1036 (36.1)	581 (23.9)	< 0.01
	Non-ideal	2070 (54.9)	2602 (54.2)		679 (33.2)	1898 (63.9)	2095 (76.1)	
BP	Ideal	1047 (36.7)	1781 (51.6)	< 0.01	1114 (61.2)	1120 (40.0)	594 (21.9)	< 0.01
	Non-ideal	2189 (63.3)	2204 (48.4)		714 (38.8)	1713 (60.0)	1966 (78.1)	
FPG	Ideal	2426 (79.4)	3513 (87.7)	< 0.01	1771 (94.6)	2391 (81.6)	1777 (68.4)	< 0.01
	Non-ideal	903 (20.6)	657 (12.3)		118 (5.4)	543 (18.4)	899 (31.6)	
Age	18-39 years	783 (41.4)	1106 (39.2)	0.01	1889 (100.0)	0 (0.0)	0 (0.0)	NA
	40-59 years	1295 (34.8)	1639 (35.5)		0 (0.0)	2934 (100.0)	0 (0.0)	
	≥ 60 years	1251 (23.8)	1425 (25.3)		0 (0.0)	0 (0.0)	2676 (100.0)	
Sex	Male	3329 (100.0)	0 (0.0)	NA	783 (50.7)	1295 (48.8)	1251 (47.8)	0.01
	Female	0 (0.0)	4170 (100.0)		1106 (49.3)	1639 (51.2)	1425 (52.2)	
Education	High	1620 (57.6)	2113 (58.1)	0.76	1474 (81.1)	1495 (51.9)	764 (28.3)	< 0.01
	Low	1709 (42.4)	2057 (41.9)		415 (18.9)	1439 (48.1)	1912 (71.7)	
Income	High	1642 (56.5)	1758 (49.9)	< 0.01	1072 (60.8)	1699 (63.4)	629 (26.6)	< 0.01
	Low	1441 (43.5)	1976 (50.1)		645 (39.2)	983 (36.6)	1789 (73.4)	
Region	Major cities	2024 (72.0)	2538 (73.0)	0.71	1284 (79.0)	1728 (68.7)	1550 (67.2)	< 0.01
	Inner	760 (20.0)	949 (19.2)		341 (15.1)	684 (21.9)	684 (23.7)	
	Other	545 (8.0)	683 (7.8)		264 (5.9)	522 (9.4)	442 (9.1)	

Numbers and percentages were expressed as unweighted and weighted and *P* values were from weighted chi-square tests. Abbreviations: CVD, cardiovascular disease; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; NA, not applicable.

Sex- and age-specific associations between individual metrics and CVD prevalence

Table 5.7 and **figure 5.2** displayed the sex-specific IRRs and PAFs between individual CVH metrics and CVD prevalence, respectively. After adjusted for covariates, high BMI, elevated BP, and elevated FPG were significant CVD risk factors in both sexes. Smoking was associated with CVD prevalence for females only and elevated TC was associated with CVD prevalence for males only. The magnitude of associations, for elevated TC ($P_{\text{interaction}} < 0.01$) and elevated BP ($P_{\text{interaction}} = 0.04$), were stronger in males than in females. Among males, high BMI ranked first among the CVD contributions (PAF = 0.297), followed by elevated TC (PAF = 0.211), elevated BP (PAF = 0.196), and elevated FPG (PAF = 0.061). High BMI was the most important CVD contributor for females (PAF = 0.130), followed by elevated BP (PAF = 0.130), smoking (PAF = 0.081), and elevated FPG (PAF = 0.066).

Table 5.8 and **figure 5.3** displayed the age-specific IRRs and PAFs between individual CVH metrics and CVD prevalence, respectively. High BMI and elevated FPG were associated with CVD prevalence in both middle-aged and older participants. Smoking, elevated BP, and physical inactivity were significant CVD risk factors for young, middle-aged and older adults, respectively. The magnitude of associations between physical inactivity ($P_{\text{interaction}} < 0.01$) and dietary pattern ($P_{\text{interaction}} < 0.01$) and CVD prevalence were diverse between age subgroups. For young adults, smoking was the only CVD contributor, and it could explain around one-third of the CVD burden (PAF = 0.329). For middle-aged adults, elevated BP was the largest CVD contributor (PAF=0.318), followed by high BMI (PAF = 0.244) and elevated FPG (PAF = 0.095). Physical inactivity was the most significant CVD contributor for older adults (PAF = 0.240), followed by high BMI (PAF = 0.112) and elevated FPG (PAF = 0.066).

Sex- and age-specific associations between overall CVH status and CVD prevalence

Table 5.9 showed the association between overall CVH status and CVD prevalence in both sexes. We observed a significant dose-response relationship between the number of ideal CVH metrics and CVD prevalence in both sexes while it is more striking in males. Compared to the participants with overall poor CVH status, those with overall intermediate and ideal CVH status, after adjusting for covariates, have a 39% and an 80% reduced CVD prevalence in males and a 26% and a 60% reduced CVD prevalence in females. One more ideal CVH metric was associated with a 27% and a 17% reduced CVD prevalence in males and females, respectively. The analyses of interaction terms implied the impacts of overall CVH status on CVD prevalence were more pronounced among males than females (P = 0.01 for interaction between sex and CVH categories; P = 0.03 for interaction between sex and the ideal metric number).

The age-specific association between overall CVH status and CVD prevalence was shown in **Table 5.9**. We noticed a significant dose-response relationship between the ideal CVH metrics number and CVD prevalence in middle-aged and older adults instead of young adults. Compared to the subjects with overall poor CVH status, those with overall intermediate and ideal CVH status, after adjusting for covariates, have a 45% and a 55% reduced CVD prevalence in middle-aged adults and a 24% and a 76% reduced CVD prevalence in older adults. One more ideal CVH metric was associated with a 25% and an 18% reduced CVD prevalence in middle-aged and older adults, respectively. The findings of interaction terms suggested overall CVH status has a similar association with CVD prevalence for the three age groups (P = 0.99 for interaction between age and CVH categories; P = 0.88 for interaction between age and the ideal metric number).

Table 5.7 IRRs between the individual CVH metrics and CVD prevalence, stratified by sex.

Metrics	Population	Crude IRR (95% CI)	*P*	Adjusted IRR* (95% CI)	*P*	$P_{interaction}$
Smoking	Males	1.65 (1.36-1.99)	< 0.01	1.12 (0.95-1.33)	0.18	0.68
	Females	1.25 (1.05-1.48)	0.01	1.20 (1.02-1.42)	0.03	
High BMI	Males	2.33 (1.80-3.01)	< 0.01	1.57 (1.29-1.92)	< 0.01	0.06
	Females	1.75 (1.47-2.10)	< 0.01	1.25 (1.05-1.49)	0.01	
Physical inactivity	Males	2.10 (1.66-2.67)	< 0.01	1.28 (0.99-1.64)	0.06	0.20
	Females	1.69 (1.33-2.13)	< 0.01	1.17 (0.91-1.50)	0.21	
Unhealthy dietary pattern	Males	0.58 (0.40-0.84)	0.01	1.31 (0.90-1.90)	0.16	0.59
	Females	1.06 (0.77-1.44)	0.73	1.08 (0.89-1.32)	0.43	
Elevated TC	Males	2.18 (1.80-2.64)	< 0.01	1.43 (1.21-1.70)	< 0.01	< 0.01
	Females	2.11 (1.75-2.56)	< 0.01	1.06 (0.88-1.27)	0.55	
Elevated BP	Males	2.14 (1.75-2.62)	< 0.01	1.36 (1.15-1.61)	< 0.01	0.04
	Females	2.51 (2.11-2.99)	< 0.01	1.27 (1.06-1.54)	0.01	
Elevated FPG	Males	2.33 (1.99-2.73)	< 0.01	1.24 (1.07-1.44)	0.01	0.59
	Females	2.44 (2.11-2.83)	< 0.01	1.45 (1.26-1.67)	< 0.01	

*Adjusted for age (continuous), education attainment, income, and residence region.

Abbreviations: CVH, cardiovascular health; CVD, cardiovascular disease; IRR, incidence risk ratio; CI, confidence interval; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

Table 5.8 IRRs between the individual CVH metrics and CVD prevalence, stratified by age.

Metrics	Population	Crude IRR (95% CI)	*P*	Adjusted IRR* (95% CI)	*P*	$P_{interaction}$
Smoking	Young adults	1.79 (1.10-2.92)	0.02	2.25 (1.18-4.29)	0.02	0.49
	Middle-aged adults	1.18 (0.95-1.46)	0.13	1.12 (0.91-1.38)	0.29	
	Older adults	1.05 (0.94-1.18)	0.36	1.05 (0.93-1.18)	0.42	
High BMI	Young adults	1.70 (0.96-3.02)	0.07	1.42 (0.77-2.62)	0.26	0.45
	Middle-aged adults	1.45 (1.14-1.85)	< 0.01	1.47 (1.14-1.90)	< 0.01	
	Older adults	1.17 (1.05-1.31)	0.01	1.17 (1.06-1.30)	< 0.01	
Physical inactivity	Young adults	1.03 (0.52-2.05)	0.93	0.76 (0.35-1.65)	0.48	< 0.01
	Middle-aged adults	1.45 (1.05-2.02)	0.03	1.20 (0.84-1.70)	0.31	
	Older adults	1.38 (1.17-1.63)	< 0.01	1.38 (1.15-1.65)	< 0.01	
Unhealthy dietary pattern	Young adults	1.66 (0.12-22.63)	0.70	1.50 (0.11-19.65)	0.75	< 0.01
	Middle-aged adults	1.06 (0.64-1.76)	0.82	0.98 (0.60-1.59)	0.92	
	Older adults	1.09 (0.90-1.31)	0.37	1.14 (0.96-1.36)	0.14	
Elevated TC	Young adults	1.63 (0.84-3.16)	0.14	1.43 (0.75-2.73)	0.28	0.81
	Middle-aged adults	1.24 (0.95-1.60)	0.11	1.13 (0.87-1.48)	0.36	
	Older adults	1.08 (0.94-1.23)	0.29	1.08 (0.94-1.23)	0.28	
Elevated BP	Young adults	1.27 (0.67-2.44)	0.46	1.35 (0.74-2.46)	0.32	0.23
	Middle-aged adults	1.86 (1.48-2.34)	< 0.01	1.77 (1.38-2.28)	< 0.01	
	Older adults	1.01 (0.88-1.16)	0.89	0.95 (0.83-1.08)	0.41	
Elevated FPG	Young adults	1.46 (0.52-4.09)	0.46	0.75 (0.13-4.41)	0.75	0.22
	Middle-aged adults	1.74 (1.37-2.22)	< 0.01	1.57 (1.24-2.00)	< 0.01	
	Older adults	1.22 (1.09-1.36)	< 0.01	1.21 (1.07-1.36)	< 0.01	

*Adjusted for age (continuous), sex, education attainment, income, and residence region.
IRR, incidence risk ratio; CVH, cardiovascular health; CVD, cardiovascular disease; CI, confidence interval; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

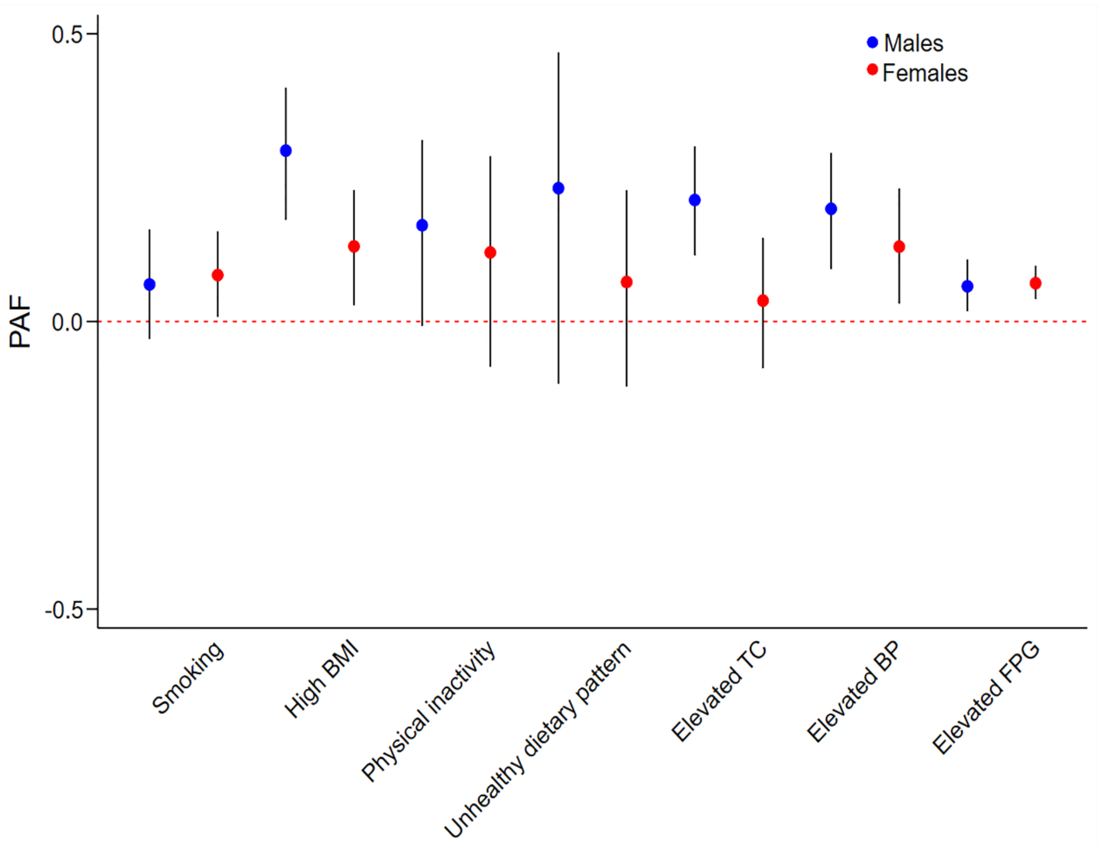

Figure 5.2 Adjusted PAFs of the CVH metrics to CVD prevalence, stratified by sex. Abbreviations: PAF, population attributable fraction; CVH, cardiovascular health; CVD, cardiovascular disease.

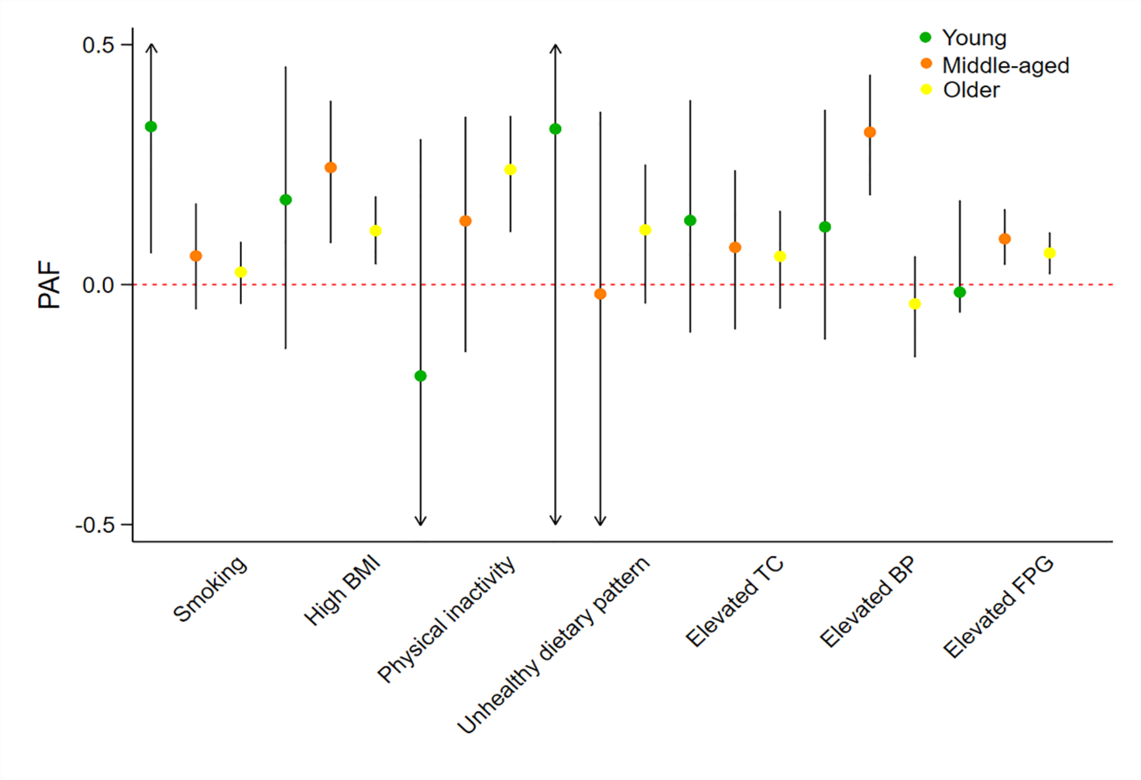

Figure 5.3 Adjusted PAFs of the CVH metrics to CVD prevalence, stratified by age. Abbreviations: PAF, population attributable fraction; CVH, cardiovascular health; CVD, cardiovascular disease.

Table 5.9 ORs between the number of ideal metrics and CVD prevalence, stratified by sex and age.

Participants	Ideal metrics number	CVD cases/participants	Crude OR (95% CI)	*P*	Adjusted* OR (95% CI)	*P*
Males	0-2	654/1741	Reference	NA	Reference	NA
	3-4	219/1147	0.34 (0.25-0.45)	< 0.01	0.61 (0.47-0.81)	< 0.01
	5-7	19/285	0.06 (0.03-0.13)	< 0.01	0.20 (0.10-0.42)	< 0.01
	One more ideal metric	NA	0.56 (0.51-0.61)	< 0.01	0.73 (0.66-0.82)	< 0.01
Females	0-2	629/1601	Reference	NA	Reference	NA
	3-4	366/1639	0.46 (0.38-0.57)	< 0.01	0.74 (0.58-0.94)	0.02
	5-7	51/589	0.11 (0.07-0.18)	< 0.01	0.40 (0.23-0.70)	< 0.01
	One more ideal metric	NA	0.61 (0.57-0.66)	< 0.01	0.83 (0.75-0.91)	< 0.01
Young	0-2	28/365	Reference	NA	Reference	NA
	3-4	50/864	0.94 (0.43-2.03)	0.86	1.20 (0.51-2.82)	0.67
	5-7	15/536	0.42 (0.16-1.12)	0.08	0.38 (0.09-1.56)	0.18
	One more ideal metric	NA	0.83 (0.66-1.03)	0.09	0.86 (0.68-1.09)	0.21
Middle-aged	0-2	377/1343	Reference	NA	Reference	NA
	3-4	195/1164	0.53 (0.42-0.68)	< 0.01	0.55 (0.42-0.73)	< 0.01
	5-7	35/256	0.34 (0.19-0.62)	< 0.01	0.50 (0.27-0.93)	0.03
	One more ideal metric	NA	0.73 (0.66-0.81)	< 0.01	0.75 (0.67-0.85)	< 0.01
Older	0-2	878/1634	Reference	NA	Reference	NA
	3-4	340/758	0.75 (0.60-0.95)	0.02	0.76 (0.60-0.96)	0.02
	5-7	20/82	0.24 (0.12-0.49)	< 0.01	0.24 (0.10-0.58)	< 0.01
	One more ideal metric	NA	0.82 (0.75-0.89)	< 0.01	0.82 (0.75-0.90)	< 0.01

*Adjusted for age (continuous), education attainment, income, and residence region for sex-specific population and additionally adjusted for sex for age-specific population.

Abbreviations: OR, odds ratio; CVD, cardiovascular disease; CI, confidence interval; NA, not applicable.

Discussion

Our study indicated that elevated BP and TC were stronger CVD risk factors for males than for females. The associations and contributions of physical inactivity on CVD prevalence were more evident among older adults than did middle-aged and young adults. For unhealthy dietary pattern, although its association with CVD prevalence was non-significant in the three age subgroups, the strength of the association was stronger in young adults. We also observed that the association between the ideal metric number and CVD prevalence was more striking among men than among woman.

Based on the results of interaction terms and PAFs, our findings, together with that of a recent Chinese cohort study, [191] suggested that high BP was more harmful to males than females, which contradicted to previous studies that have reported similar association in both sexes [192] or stronger association in females. [193-196] One possible explanation of the different conclusions is the definitions of non-ideal BP status in each study. For instance, one study defined non-ideal BP as self-reported hypertension or BP ≥ 140/90 mm Hg [195] while our study used BP ≥ 120/80 mm Hg instead. Besides, our study did not include medication for high BP in the definition. We also noticed a stronger adverse influence of increasing TC level in men than in women, which was supported by recent studies. [193, 197] A recent cohort study also indicated the more pronounced effects of TC on MI in males (IRR: 1.19) than in females (IRR: 1.12). [193] A large-scale meta-analysis also observed a stronger effect of 1 mmol/L elevated TC in men (RR: 1.24) compared to women (RR: 1.20). [197] We found that the association between physical inactivity and CVD prevalence was more obvious among older adults compared to young and middle-aged adults (*P* for interaction < 0.01). Also, physical inactivity contributed to 24.0% CVD burden in older adults whereas it was not a significant CVD contributor in young and middle-aged adults. The greater impact of physical activity on CVD prevalence among older adults was in agreement with previous reports. [194, 195] The INTERHEART study observed that self-reported physical activity was associated with more significant reductions in the odds of MI in those aged 60 years or over compared to those younger than 60 years and the age variances were consistent in both males and females. [194] The INTERSTROKE study revealed that self-reported physical inactivity was a slightly stronger stroke contributor in older adults (> 55 years) compared with young adults (≤ 55 years) (PAF: 35.9% versus 35.3%). [195] We reported that the magnitude of the association between dietary pattern and CVD prevalence was more apparent in young adults, although the association failed to reach a statistically significant level in all the three age groups. Similarly, a large-scale Chinese cohort indicated one daily portion of fresh fruit was associated with a 45% cardiovascular deaths reduction in those aged 35-59 years while the proportion reduced to 25% and 39% for those aged 60-69 years and 70-79 years, respectively. [198] Nevertheless, contradicted to our findings, another study revealed that diet played a more significant role in the development of stroke among older adults. [195] The variations in dietary pattern components and the age classifications across the studies could partly account for the inconsistent conclusions. Although we failed to detect the sex and age variations in the magnitude of associations and contributions between other CVH metrics and CVD prevalence, previous studies, however, suggested the existence of possible sex and/or age disparities. For example, two recent meta-analyses indicated that female smokers had a higher risk of CHD and stroke than male smokers did. [199, 200] The impact of high BMI on the risk of IHD and stroke, as reported by another study, has attenuated with age. [17] Hence, we still need further explorations for the sex and age-specific associations between CVH metrics and CVD risk to prioritize CVD prevention strategies.

We observed that the increased ideal CVH metrics number was significantly associated with reduced CVD prevalence in most sex and age subgroups and the dose-response fashion was also noticed in a few recent meta-analyses. [14, 141] The number of ideal metrics has more significant influences on CVD prevalence in men compared with women in our study. Two studies indicated the association strengths between the number of ideal CVH metrics and HF incidence/asymptomatic ICAS prevalence were similar in both sexes [91, 145] whereas several studies found that males are more likely to influenced by the CVH metrics for CVD events [29, 150] and stroke. [42] The different risk factor profiles of CVD subtypes, study designs (cohort versus cross-sectional), and outcomes (incidence/mortality versus prevalence) could partially explain the conflicting conclusions. Several sex-specific CVD risk factors may also contribute to the variations. For example, it has been reported that both gestational diabetes mellitus [201] and hypertensive disorders of pregnancy [202] could substantially raise the CVD risk in females. The findings of interaction terms indicated that the ideal metrics number has similar association with CVD prevalence across the three age subpopulations. Few studies focused on the age differences in the associations between the number of ideal CVH metrics and risk of CVD-related events while they reached inconclusive findings. [42, 91, 145] A cohort study in the US suggested that the ideal CVH metrics number played a stronger role in the risk of HF incidence among those aged < 65 years compared with those aged 65 or over. [91] A Chinese cross-sectional study indicated the impacts of CVH metrics number on asymptomatic ICAS prevalence was more evident in older adults (≥ 60 years) than in middle-aged adults (40-59 years). [145] However, a Chinese cohort study demonstrated that the magnitude of the association between the CVH metrics number and stroke incidence was stronger in middle-aged adult (40-59 years) compared with older adults (≥ 60 years). [42] Thus, whether age played a role in the association between CVH metrics and CVD prevalence is still unclear, and the topic warrants further explorations.

To the best of our knowledge, our study firstly explored the possible sex and age variances in the associations between AHA's CVH metrics and CVD prevalence in Australian adults. The present study was among one of the few studies that focused on the sex- and age-specific associations between CVH metrics and CVD risk globally. As CVD is the leading cause of deaths in Australia, [1] it could provide clues for the strategies of CVD risk reduction in Australian sex and age subgroups. The National Vascular Disease Prevention Alliance released the guidelines for CVD risk management in 2012, and it focused on the Australian adults aged 45 or over and it lacked the detailed information on the measurements of CVH status in the general population. [10] Since our results showed that young adults are also suffering from poor CVH status, we recommend including young adults as a target population for future CVD prevention guidelines. The AHA's 2020 Impact Goal was not only used in the American subjects but also commonly used in populations across the world. [203] When compared to CVH status from adults worldwide, [203] the Australian adults have a lower prevalence of ideal status for most metrics, and poorer overall CVH status and the results were generally consistent in all age and sex subgroups. Since the AHA's 2020 Impact Goal was to improve CVH of all Americans by 20%, [7] the goal of CVH improvement should be even greater in Australia and, therefore, the promotion of modifiable lifestyles in the general Australian adults are urgently needed. Since the AHS excluded the indigenous Australians, we need more studies to describe CVH status and its association with CVD risk among indigenous communities. Additionally, more cohort studies and interventional studies should be implemented to estimate the long-term effects of those modifiable metrics on CVD risk.

We should notice some limitations to our study. Firstly, although we used a nationally representative sample and applied the biomedical weight, we may still suffer from the selection bias as we noticed the differences for some demographic factors and CVH metrics between participants and non-participants (**Table 4.2**). Secondly, our study was a cross-sectional study, and we could not establish the causal relationship between CVH metrics and CVD risk. It is unable to explore the sex and age disparities in the effects of CVH metrics on CVD incidence or mortality. It could also induce reverse causality as those diagnosed with CVD may take lifestyle modifications or medicines, and it may bias the associations between CVH metrics and CVD prevalence. Thirdly, we modified the classification criteria of some metrics, when compared to the AHA's classifications, based on our dataset, which may lead to classification bias. Fourthly, as most of the CVD types in our study were coded as other CVDs, we are unable to provide age- and sex-specific prevalence and risk factors for CVD subtypes. Besides, we used self-reported CVD prevalence, and it may underestimate or overestimate the CVD prevalence. Other variables, including demographic factors, smoking, dietary pattern, and physical activity, were also self-reported and they may not be entirely accurate.

CONCLUSIONS

Our results suggested that the associations and contributions of elevated BP, elevated TC and the ideal CVH metrics number on CVD prevalence were more pronounced in males than in females. Physical inactivity and dietary pattern played a more significant role in CVD prevalence among older and young adults, respectively. Population-based and sex/age-specific strategies should be implemented to promote CVH status and reduce the burden of CVD in Australian adults.

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Contributors YP and ZW conceived and designed the study. YP acquired, analysed and interpreted the data. YP drafted the paper. ZW critically revised the paper. All authors have read and approved the final version for publication.

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Chapter 6 – The CVH status and IHD prevalence in Australian adults

Chapter 3 has summarized the findings on the associations between the CVH status the IHD risk. As a result, few studies have focused on the effects of Life's Simple 7 and IHD risk. Thus, we examined the separate and combined associations between the CVH status and IHD prevalence in overall Australian adults using the core sample of the 2011-2012 AHS (Chapter 6.1). The sex and age variations in the magnitude of the association were also explored (Chapter 6.2). This chapter addressed the research objective 5 of the thesis.

6.1 The CVH status and IHD prevalence in the overall Australian adults

This section was formatted as the following publication:

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Bin Dong	Data analysis and result interpretation (10%) Reviewing of article (30%)
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Odewumi Adegbija	Data analysis and result interpretation (10%) Reviewing of article (10%)

Life's Simple 7 and ischemic heart disease in the general Australian population

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Abstract

Background: The AHA released 7 modifiable factors, Life's Simple 7, that are expected to improve the CVH, but their contributions to IHD prevalence in the general Australians are not well clarified.

Methods: We performed a cross-sectional study based on 7499 adults (≥18 years) who have tested for TC and FPG as part of the 2011-2012 AHS. The exposures included seven CVH metrics and overall CVH status, defined by the number of ideal metrics. The outcome was the self-reported IHD prevalence. Poisson regression analyses were used to estimate the IRRs and PAFs of those factors to IHD prevalence. Participants were classified into three CVH groups based on the number of ideal metrics: inadequate (0-2), average (3-4), and optimal (5-7). Logistic regression analyses were performed to elucidate the relationship between the overall CVH and IHD prevalence.

Results: 357 participants were self-reported having IHD condition, with a weighted prevalence of 3.3%. Physical inactivity, elevated BMI and TC were independently associated with IHD prevalence. Compared to the inadequate category, participants in the optimal and average categories have a 78% (adjusted OR, 0.22; 95% CI, 0.03-1.96) and a 45% (adjusted OR, 0.55; 95% CI, 0.39-0.77) lower IHD prevalence. One more optimal metric was associated with an 18% lower IHD prevalence (adjusted OR, 0.82; 95% CI, 0.71-0.93).

Conclusions: Our findings indicate that physical inactivity, raised BMI, and elevated TC were independent modifiable risk factors of IHD prevalence in the general Australian population. The improvement of the overall CVH may also reduce IHD prevalence among the general Australian adults.

Introduction

IHD, one of the most popular CVDs, accounted for 13.3% of global all-causes of death in 2010 and the proportion has increased by more than one third compared to that in 1990. [170] IHD ranked first in causes of both death and years of life lost (YLLs) worldwide. [140] In Australia, IHD is also one of the leading contributors to mortality and YLLs. It was reported that 17.9% of all-cause mortality was due to IHD among Australians. [204] According to the 2013 Global Burden of Disease Study, IHD was the leading cause of YLLs in Australia. [19]

To measure and improve the CVH in the general American population, the AHA recommended seven modifiable factors, also called Life's Simple 7, namely are smoking status, BMI, physical activity, dietary pattern, TC, BP, and FPG. [7] In a nationally representative survey of US, most of the metrics were significantly associated with risk of IHD mortality and there is a negative association between the number of ideal metrics and IHD mortality. [30] The strong associations between Life's Simple 7 and incidence of CHD, another term of IHD, are noticed in several cohort studies in Europe [84] and China. [113] The associations between Life's Simple 7 and IHD risk were still not well examined in the general Australian adults.

Our current study was based on an Australian representative sample, the core sample of the AHS, aiming to clarify the separate and combined associations between Life's Simple 7 and IHD prevalence. We hypothesized that, in Australian adults, most CVH metrics were associated with IHD prevalence and there is a negative association between number of ideal metrics and IHD prevalence.

Subjects and Methods

Study Design and Subjects

We used data from the core sample of the 2011-2012 AHS, a national wide and population-based survey consisting of three arms: a general health survey, a nutrition and physical activity survey, and a voluntary biomedical survey which included participants from the first two arms. The survey was conducted using a stratified multistage sample that is representative of the general Australian population. Households that were living in very remote areas of Australia and discrete Aboriginal and Torres Strait Islander communities were not in scope. The core sample consisted of 24910 adults (≥ 18 years old). We restricted our study to those with TC and FPG (n=7499). All participants provided written informed consent and our study was approved by The School of Medicine Low Risk Ethical Review Committee in the University of Queensland (approval number 2016-SOMILRE-0161).

Life's Simple 7

Individual modifiable factors were categorized as ideal and unideal, respectively. For smoking status, the participants were categorized into current/former smokers (unideal) and never smokers (ideal). For BMI status, participants were classified into the ideal category if they had BMI values less than 25 kg/m^2. Participants were regarded as having an ideal physical activity status if they had taken 150 minutes moderate, 75 minutes vigorous or 150 minutes combined moderate and vigorous physical activity last week. We included two dietary factors, usual daily intake of fruits and vegetables, in our analyses. Participants were categorized as having an ideal dietary pattern if they had sufficient fruits and vegetables intake, which was determined by 2013 Australian Dietary Guidelines. Participants were considered to have an ideal TC status if they had TC concentration < 200 mg/dL and were not taking cholesterol-lowing medication. Participants were considered to have an ideal BP status if they had systolic BP <120 mmHg and diastolic BP <80 mm Hg. For FPG, a value less than 100 mg/dL was considered as ideal status. We used the number of ideal metrics to measure the overall CVH and participants were divided into three groups (0-2, 3-4 and 5-7 ideal metrics), accordingly. [27]

Outcome Measurement

The self-reported IHD prevalence was based on ICD-10, codes I20-I25. To be more specific, respondents were regarded as having an IHD condition if they had been told by a doctor or nurse that they had IHD and they currently have IHD while taking the survey.

Covariates

The following variables were adjusted as covariates in our study: age (continuous), sex, education attainment, income status, and residence region. Education attainment was categorized as high (≥ 12 school years) and low (< 12 school years). Income status was evaluated by household income and dichotomized as low (≤ 50th percentile equivalised weekly household income) and high (> 50th percentile equivalised weekly household income). Residence region was classified into major cities, inner regional areas and other areas (outer regional and remote). They were included in the multivariate models along with the individual metric, the number of ideal metrics or CVH categories.

Statistical analysis

Firstly, we applied univariate and multivariate Poisson regression analysis to obtain the crude and adjusted IRRs and corresponding 95% CIs and they were used to measure the associations between modifiable factors and IHD occurrence.

Secondly, we calculated adjusted PAFs based on the following equation to quantify the effects of each component on IHD reduction. [172] *Pe* is the prevalence of exposure and RRs were replaced with adjusted IRR. Participants with available CVH metrics were included in the first and second analyses for specific metrics.

$$PAF = \frac{Pe \times (RR - 1)}{1 + Pe \times (RR - 1)}$$

Thirdly, we calculated ORs and 95% CIs using logistic regression analyses to explore the relationship between the overall CVH and IHD prevalence. We treated the number of ideal metrics as a continuous and a categorical variable, respectively. Participants with missing values in one or more of Life's Simple 7 components were not included in the analyses.

Biomedical weights were applied, using the Jackknife method, as recommended by the ABS to representative the in-scope population. All analyses used expanded confidentialised unit record files of the AHS core sample and were conducted within the ABS's RADL with Stata, version 10.0. A two-sided P value < 0.05 was considered statistically significant.

Results

Among the 7499 eligible participants, 357 were positive for IHD occurrence and the weighted prevalence was 3.3%. For the seven metrics, FPG had the highest weighted ideal prevalence (83.6%), followed by smoking status (55.6%), BP (44.2%), BMI (39.2%), TC (45.5%), physical activity (26.7%) and dietary pattern (4.8%). The details of metrics and covariates are summarized in **Table 6.1**.

Table 6.1 Distribution of IHD cases, stratified by the metrics and covariates.

Variables	Status	IHD, n (%) [a]	Non-IHD, n (%) [a]	P [b]
Smoking	Ideal	132 (2.5)	3630 (97.5)	< 0.01
	Unideal	225 (4.3)	3512 (95.7)	
BMI	Ideal	71 (1.9)	2324 (98.1)	< 0.01
	Unideal	262 (4.1)	4470 (95.9)	
Physical activity	Ideal	35 (1.0)	1739 (99.0)	< 0.01
	Unideal	322 (4.1)	5399 (95.9)	
Dietary pattern	Ideal	22 (3.6)	412 (96.4)	0.72
	Unideal	335 (3.3)	6730 (96.7)	
TC	Ideal	64 (1.5)	2763 (98.5)	< 0.01
	Unideal	293 (4.8)	4379 (95.2)	
BP	Ideal	96 (1.9)	2732 (98.1)	< 0.01
	Unideal	246 (4.5)	4147 (95.5)	
FPG	Ideal	214 (2.5)	5725 (97.5)	< 0.01
	Unideal	143 (7.3)	1417 (92.7)	
Age	< 60 years	72 (1.1)	4751 (98.9)	< 0.01
	≥ 60 years	285 (10.2)	2391 (89.8)	
Sex	Male	214 (4.2)	3115 (95.8)	< 0.01
	Female	143 (2.5)	4027 (97.5)	
Education level	High	80 (1.6)	3653 (98.4)	< 0.01
	Low	277 (5.7)	3489 (94.4)	
Income	High	73 (1.6)	3327 (98.4)	< 0.01
	Low	257 (5.8)	3160 (94.2)	
Region	Major cities	178 (2.6)	4384 (97.4)	< 0.01
	Inner regional	114 (5.1)	1595 (94.9)	
	Other	65 (5.4)	1163 (74.6)	

[a] Numbers and percentages were presented as unweighted and weighted, respectively.
[b] *P* values were from weighted chi-square tests.
Abbreviations: IHD, ischemic heart disease; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

In the univariate analysis, all the seven components, except for dietary pattern, were positively associated with increased IHD prevalence. After adjusted for confounders, physical inactivity (adjusted IRR: 2.10; 95% CI: 1.28-3.45, P<0.01), unideal TC (adjusted IRR: 1.58; 95% CI: 1.10-2.25, P=0.01) and elevated BMI (adjusted IRR: 1.40; 1.05-1.87, P=0.02) were still significantly associated with raised IHD risk (**Table 6.2**). We calculated adjusted PAFs to quantify the relative contributions of target influencing factors to IHD prevalence (**Figure 6.1**). Insufficient physical activity was the largest contributor to IHD prevalence (adjusted PAF: 46%; 95% CI: 0.18-0.65), followed by elevated TC (adjusted PAF: 26%; 95% CI: 0.06-0.44), and elevated BMI (adjusted PAF: 21%; 95% CI: 0.03-0.37).

Table 6.2 IRRs between the individual CVH metrics and IHD prevalence in the overall population.

Variables	Crude IRR (95% CI)	*P*	Adjusted[a] IRR (95% CI)	*P*
Smoking	1.70 (1.25-2.30)	< 0.01	1.22 (0.89-1.67)	0.22
Elevated BMI	2.16 (1.58-2.94)	< 0.01	1.40 (1.05-1.87)	0.02
Physical inactivity	3.92 (2.39-6.45)	< 0.01	2.10 (1.28-3.45)	< 0.01
Unideal dietary pattern	0.90 (0.50-1.62)	0.73	1.21 (0.71-2.07)	0.48
Elevated TC	3.25 (2.28-4.64)	< 0.01	1.58 (1.10-2.25)	0.01
Elevated BP	2.33 (1.61-3.39)	< 0.01	0.83 (0.58-1.18)	0.29
Elevated FPG	2.86 (2.13-3.84)	< 0.01	1.19 (0.84-1.68)	0.32

[a] Adjusted for age (continuous), sex, education attainment, income, and residence region.
Abbreviations: IRR, incidence rate ratio; CVH, cardiovascular health, IHD, ischemic heart disease; CI, confidence interval; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

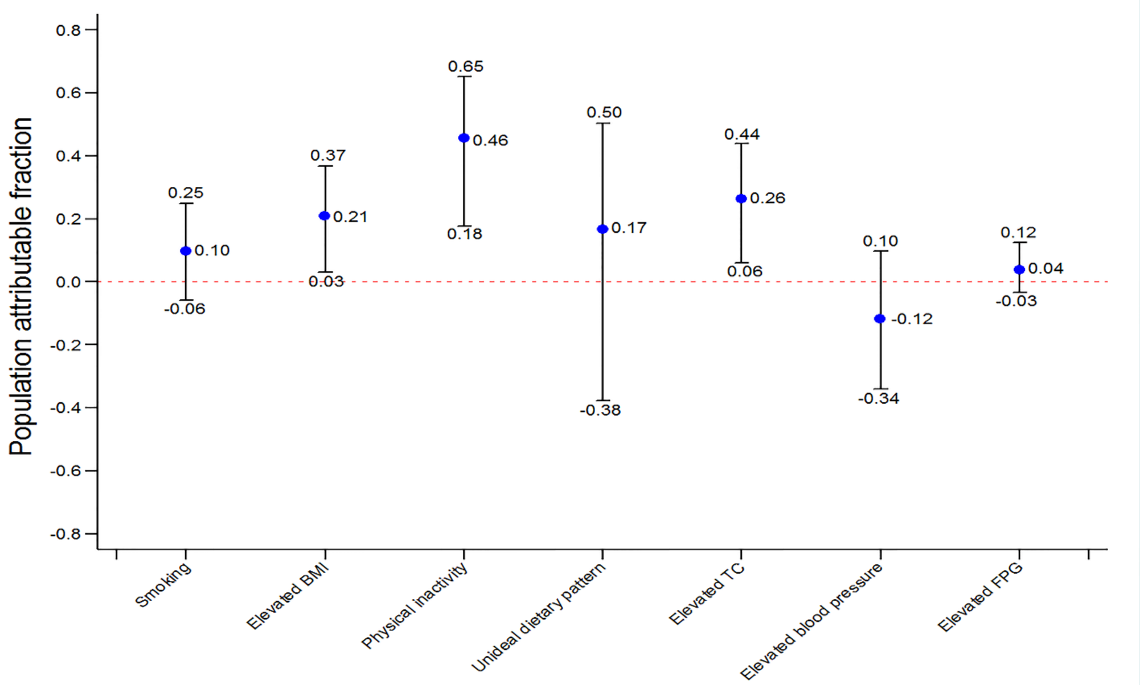

Figure 6.1 Adjusted PAFs of the CVH metrics to IHD prevalence in the overall population. Abbreviations: TC, total cholesterol; FPG, fasting plasma glucose; CVH, cardiovascular health; IHD, ischemic heart disease.

Table 6.3 shows the relationship between Life's Simple 7 overall categories and IHD prevalence. Compared to those in the inadequate category, those in the optimal category had a 78% lower risk of IHD (adjusted OR: 0.22; 95% CI: 0.03-1.96) and those in the average category had a 45% lower risk (adjusted OR: 0.55; 95% CI: 0.39-0.77). On average, one more ideal metric was associated with an 18% lower risk of IHD prevalence (adjusted OR: 0.82; 95% CI: 0.71-0.93).

Table 6.3 ORs between the number of ideal metrics and IHD prevalence in the overall population.

Ideal metrics number	IHD cases/participants	Crude OR (95% CI)	*P*	Adjusted [a] OR (95% CI)	*P*
0-2	241/3342	Referent	--	Referent	--
3-4	73/2786	0.28 (0.19-0.41)	< 0.01	0.55 (0.39-0.77)	< 0.01
5-7	4/874	0.03 (0.00-0.23)	< 0.01	0.22 (0.03-1.96)	0.17
One more ideal metric	--	0.56 (0.50-0.63)	< 0.01	0.82 (0.71-0.93)	< 0.01

[a] Adjusted for age (continuous), sex, education attainment, income, and residence region.

Abbreviations: IHD, ischemic heart disease; OR, odds ratio; CI, confidence interval.

Discussion

To the best of our knowledge, it is the first study that explored the individual and combined effects of Life's Simple 7 on IHD prevalence among the general Australians. We observed that physical inactivity, elevated BMI and raised TC are independent risk factors of IHD prevalence. The higher optimal metric number was associated with reduced IHD prevalence.

Physical inactivity was the most significant contributor to IHD prevalence in our study, with adjusted PAF of 46%. A recent meta-analysis revealed that, compared with insufficiently active participants (reporting less than 600 MET (Metabolic Equivalent) minutes/week of total physical activity), the risk of IHD among those in the low active (600-3999 MET-minutes/week), moderately active (4000-7999 MET-minutes/week), and highly active (⩾8000 MET-minutes/week) categories has reduced by 16%, 23%, and 25%, respectively. [205] In our study, less than 1 out of 4 participants met the requirement of physical activity. Thus, the policy makers should pay greater attention to the physical activity promotion in general Australians.

High BMI was observed as a significant influencing factor of IHD, which is in agreement with several studies. A large-scale collaborative analysis identified one standard deviation (4.56 kg/m^2) increase in BMI was independently associated with 11% higher risk of CHD incidence. [206] Another collaborative study demonstrated the positive relationship between BMI and IHD mortality. [207] It observed that, in the upper range of BMI (25-50 kg/m^2), each 5 kg/m^2 higher BMI was associated with a 39% higher IHD mortality.

We also found the independent and positive relationship between TC and IHD prevalence. A recent meta-analysis of more than one million persons from 97 prospective studies indicated that each one mmol/L increase in TC raised the risk of CHD incidence by 24% and 20% in male and female, which is consistent with our findings. [197] While, a recent study, using NHANES data, found a non-significant relationship between TC and IHD mortality. [30] Given the conflicting findings, more researches on the TC-IHD relationship are warranted.

Smoking, elevated BP, and raised FPG were significant IHD contributors in the unadjusted analysis. However, the associations were attenuated after adjustment for several socio-economic factors (**Table 6.2**). The potential role of those socio-economic variables on CVD risk was indicated by several previous studies. [3, 208-210] Also, the IHD prevalence varied by the status of those factors in the current study (**Table 6.1**). We failed to detect the role of dietary pattern in both univariate and multivariate models, which is in agreement with several studies. [27, 84, 144] While, others displayed its role in CVD risk reduction. [29, 42] The different measurements of dietary pattern may partially explain the conflicting findings. Another possible explanation is the non-IHD group contained participants with other types of CVD and it could underestimated the associations between the CVH metrics and IHD prevalence in our study. The secondary prevention in IHD patients is another possible reason for the phenomenon. However, we can observe that IHD patients have lower prevalence of ideal status for most metrics compared to non-IHD patients. In addition, some key indicators of IHD secondary preventions, such as medications for hypertension and diabetes, were missing. We could not imply that the risk management among IHD patients was successful.

We have found that the higher number of ideal metrics was greatly related to IHD risk reduction. Our findings are consistent with several previous studies, which also found the inverse relationship between the overall CVH and CVD risk. [63, 143] Our results suggested that some components may not individually relate to IHD prevalence, but they are likely to interrelate with other Life's Simple 7 metrics and have synergistic effects on IHD prevalence.

Our study has some limitations. First, it is a cross-sectional study and we are unable to examine the temporality between influencing factors and IHD incidence or mortality. Second, we used modified metric definitions compared to those outlined by the AHA [7] due to dataset structures, and the modifications may make our results incomparable to other studies. For example, the AHA guideline consisted five components for dietary assessment. [7] However, our study only included fruits and vegetables as other components were not available in the AHS. Thirdly, we did not compare the IHD risk differences for those in the same CVH groups giving the limited sample size. Fourthly, 17.7% of the total participants were self-reported CVD other than IHD, and they were classified as non-IHD group in our study. It may underestimate the associations between Life's Simple 7 and IHD prevalence. Fifth, as there is very limited studies on the Life's Simple 7 and IHD prevalence globally, it is difficult to make comparisons between our findings with others. Sixth, although the AHS is a nationally representative survey and we used biomedical weight, we are still suffering from the risk of selection bias as we noticed some differences for some demographic factors and CVH metrics between participants and non-participants (**Table 4.2**). In addition, some variables, like dietary pattern, smoking status, and the IHD status, were self-reported and thus may bring about misclassifications.

Conclusions

In summary, we observed physical inactivity, high BMI, and elevated TC as significant risk factors and contributors to IHD prevalence in the general Australian adults. The higher number of optimal Life's Simple 7 metrics was associated with a lower risk of IHD prevalence.

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6.2 The CVH status and IHD prevalence in the Australian sex and age subgroups

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Contributor	Statement of contribution
Yang Peng (Candidate)	Conception and design (70%) Data analysis and result interpretation (100%) Drafting of article (100%) Reviewing of article (50%)
Zhiqiang Wang	Conception and design (30%) Reviewing of article (50%)

Could the Cardiovascular Health Metrics Account for the Age and Sex Disparities in Self-Reported Ischemic Heart Disease Prevalence?

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Abstract: The AHA has outlined seven modifiable CVH metrics. However, the sex and age disparities in the association between those CVH and IHD risk are unclear. Our study sought to examine the possible sex and age variations in the association between the CVH metrics and IHD prevalence using an Australian nationally representative survey. We used the core sample of the 2011-2012 AHS, and 7499 adults with FPG and TC values were included. We used Poisson regression analysis to measure the associations between individual metrics and IHD prevalence. Our study used both stratification and interaction analyses to compare the magnitude of associations between sex and age groups. Then, we calculated the PAFs to measure the contribution of each metric to IHD prevalence. In addition, we applied logistic regression analysis to examine the influences of the ideal CVH metrics number on IHD prevalence and used stratification and interaction analyses. BMI, physical activity, BP, and FPG have greater effects on IHD prevalence in young adults compared to older adults. We failed to detect sex variations in CVH metrics and IHD prevalence. The ideal CVH metrics number was inversely correlated to IHD prevalence and it has similar effects in four subgroups. These CVH metrics do not explain the sex and age disparities in IHD prevalence and the topic needs further explorations.

Keywords: cardiovascular health; ischemic heart disease; Australian adults

Introduction

IHD is one common type of CVD and is a significant contributor to deaths worldwide. According to the Global Burden of Disease Study, IHD led to nearly 10 million deaths worldwide in the year 2016, which accounted for 17.3% of all deaths. [1] There is evidence that a large proportion of IHD burden could be attributable to modifiable factors. A Chinese cohort found that almost half of the IHD cases could be prevented if the participants adhered to six healthy lifestyle factors, including smoking, alcohol consumption, physical activity, dietary pattern, and BMI. [5] In a US study, six lifestyle factors could explain 73% of CHD, another term for IHD, events in a 20-years follow-up period. [6]

The AHA has outlined seven modifiable metrics (smoking, BMI, physical activity, dietary pattern, TC, BP, and FPG) to define and monitor the CVH status in the general population. [7] Some studies have reported that the ideal status of those metrics played a crucial role in the reduction of IHD risk. [30, 152] A few studies have suggested that the strengths of association between modifiable factors and IHD risk differed by age and sex [211, 212] while the variations were inconclusive due to very limited studies.

In our study, we analysed and compared the strengths of association between the CVH metrics and IHD prevalence in sex and age-specific subpopulations using a nationally representative survey in Australia. We hypothesized that the CVH metrics played a more significant role in IHD prevalence among males and older adults.

Methods

Study design and participants

Details of the study design and participants have been described previously. [152] Briefly, our study used the core sample of the 2011-2012 AHS, which is a nationally representative health survey of the general Australians. Among 24910 adults (≥ 18 years), we focused on those with available TC and FPG results, yielding to an overall sample size of 7499. Participants were classified into two age groups: young (< 60 years) and older (≥ 60 years).

CVH metrics

The definitions of the seven CVH metrics were described elsewhere. [152] Subjects with 0-2, 3-4, and 5-7 ideal metrics were regarded as having overall poor, intermediate, and ideal CVH status. [84]

Outcome measurement

The IHD prevalence was self-reported and based on the 10^{th} version of ICD, codes I20-I25. To be more specific, participants were asked if they had been told by a doctor or nurse that they had IHD and they currently have IHD while taking the survey. They would be regarded as positive for IHD if they answered “yes” to both questions.

Covariates

The following variables were adjusted as covariates in our study: age (continuous), sex, education attainment, income status, and residence region. Education attainment was categorized as high (≥ 12 school years) and low (< 12 school years). Income status was evaluated by household income and dichotomized as low (≤ 50th percentile equivalised weekly household income) and high (> 50th percentile equivalised weekly household income). Residence region was classified into major cities, inner regional areas and other areas (outer regional and remote).

Statistical analysis

Firstly, we compared the proportions of IHD, ideal metrics, and covariates between sex and age groups using weighted chi-square tests.

Secondly, we explored the possible sex and age variations in the associations and contributions of individual metrics and IHD prevalence. We calculated crude (unadjusted) and adjusted IRRs and corresponding 95% CIs, using univariate and multivariate Poisson regression analyses, to clarify the association between the CVH metrics and IHD prevalence in each sex and age-specific group. We entered the interaction terms between sex/age and metrics in the adjusted models to explore the potential sex/age differences in the association.

Additionally, we calculated adjusted PAFs, for each sex and age group, based on the following equation to measure the effects of each metric on IHD reduction. *Pe* is the prevalence of unideal metric and RRs were replaced with adjusted IRRs.

$$PAF = \frac{Pe \times (RR - 1)}{1 + Pe \times (RR - 1)}$$

Thirdly, we calculated ORs using logistic regression analyses to explore the relationship between the overall CVH status categories and IHD prevalence in sex and age subgroups. Interaction terms between sex/age and the CVH categories were included in the adjusted models. Participants with missing values in at least one CVH metrics were not included in the analyses.

To infer results for the in-scope population, we used biomedical weight and group Jackknife method with 60 replicate weights in the CVH metrics and IHD association analyses. All analyses were conducted within the ABS's RADL with Stata 10.0. A two-tailed *P*-value < 0.05 was used to determine statistical significance.

Results

Baseline characteristics

The basic characteristics of the included participants were displayed in **Table 6.4**. Overall, weighted 3.3% participants were positive for IHD prevalence (357/7499). Males have higher IHD prevalence than did the females (4.2% versus 2.5%, $P<0.01$) and older adults have statistically higher IHD prevalence when compared to young adults (10.2% versus 1.1%, $P<0.01$). Females have higher proportions of ideal smoking, BMI, dietary pattern, BP, and FPG and lower ideal physical activity proportion and income status than did males. They have similar ideal TC prevalence, education level, and regional distribution. Compared to young adults, older adults had a significantly higher percentage of ideal dietary pattern and lower prevalence of ideal status for the other six metrics. Young adults have higher income and education level and more likely to reside in major cities as compared to older adults.

Table 6.4 Baseline characteristics of the included participants.

Metrics	Status	Males, n (%)	Females, n (%)	*P*	Young, n (%)	Older, n (%)	*P*
IHD	Yes	214 (4.2)	143 (2.5)	< 0.01	72 (1.1)	285 (10.2)	< 0.01
	No	3115 (95.8)	4027 (97.5)		4751 (98.9)	2391 (89.8)	
Smoking	Ideal	1420 (49.8)	2342 (61.1)	< 0.01	2521 (57.7)	1241 (49.0)	< 0.01
	Non-ideal	1909 (50.2)	1828 (38.9)		2302 (42.3)	1435 (51.0)	
BMI	Ideal	833 (32.3)	1562 (46.2)	< 0.01	1750 (43.1)	645 (27.2)	< 0.01
	Non-ideal	2388 (67.7)	2344 (53.8)		2843 (56.9)	1889 (72.8)	
Physical activity	Ideal	945 (32.7)	829 (20.9)	< 0.01	1320 (30.0)	454 (16.6)	< 0.01
	Non-ideal	2382 (67.3)	3339 (79.1)		3500 (70.0)	2221 (83.4)	
Dietary pattern	Ideal	93 (2.1)	341 (7.4)	< 0.01	223 (4.1)	211 (6.9)	< 0.01
	Non-ideal	3236 (97.9)	3829 (92.6)		4600 (95.9)	2465 (93.1)	
TC	Ideal	1259 (45.1)	1568 (45.8)	0.70	2246 (52.5)	581 (23.9)	< 0.01
	Non-ideal	2070 (54.9)	2602 (54.2)		2577 (47.5)	2095 (76.1)	
BP	Ideal	1047 (36.7)	1781 (51.6)	< 0.01	2234 (51.4)	594 (21.9)	< 0.01
	Non-ideal	2189 (63.3)	2204 (48.4)		2427 (48.6)	1966 (78.1)	
FPG	Ideal	2426 (79.4)	3513 (87.7)	< 0.01	4162 (88.6)	1777 (68.4)	< 0.01
	Non-ideal	903 (20.6)	657 (12.3)		661 (11.4)	899 (31.6)	
Age	< 60 years	2078 (76.2)	2745 (74.7)	0.01	4823 (100.0)	0 (0.0)	NA
	≥ 60 years	1251 (23.8)	1425 (25.3)		0 (0.0)	2676 (100.0)	
Sex	Male	3329 (100.0)	0 (0.0)	NA	2078 (49.8)	1251 (47.8)	0.01
	Female	0 (0.0)	4170 (100.0)		2745 (50.2)	1425 (52.2)	
Education level	High	1620 (57.6)	2113 (58.1)	0.76	2969 (67.5)	764 (28.3)	< 0.01
	Low	1709 (42.4)	2057 (41.9)		1854 (32.5)	1912 (71.7)	
Income	High	1642 (56.5)	1758 (49.9)	< 0.01	2771 (62.0)	629 (26.6)	< 0.01
	Low	1441 (43.5)	1976 (50.1)		1628 (38.0)	1789 (73.4)	
Region	Major cities	2024 (72.0)	2538 (73.0)	0.71	3012 (74.2)	1550 (67.2)	< 0.01
	Inner regional	760 (20.0)	949 (19.2)		1025 (18.3)	684 (23.7)	
	Other	545 (8.0)	683 (7.8)		786 (7.5)	442 (9.1)	

Numbers and percentages were expressed as unweighted and weighted and *P* values were from weighted chi-square tests. Abbreviations: IHD, ischemic heart disease; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; NA, not applicable.

Sex- and age-specific associations between individual metrics and IHD prevalence

Table 6.5 and **Table 6.6** list the sex and age-specific crude and adjusted IRRs and 95% CIs by the CVH metric for IHD prevalence, respectively. After adjusted for covariates, physical inactivity (IRR: 1.84, 95% CI: 1.00-3.39, *P*=0.048) and elevated TC values (IRR: 1.53, 95% CI: 1.04-2.25, *P*=0.03) were significant IHD risk factors for males. None of the metrics was associated with IHD prevalence for females. For the analyses of interaction terms, we failed to detect the sexual differences in the associations between those metrics and IHD prevalence ($P_{\text{interaction}} > 0.05$). Physical inactivity (IRR: 1.63, 95% CI: 1.01-2.64, *P*=0.046) and elevated TC (IRR: 1.67, 95% CI: 1.11-2.51, *P*=0.02) were significant IHD risk factors for older adults. None of the metrics was associated with IHD prevalence for young adults. The effects of high BMI ($P_{\text{interaction}} = 0.01$), physical inactivity ($P_{\text{interaction}} = 0.03$), elevated BP ($P_{\text{interaction}} < 0.01$), and elevated FPG ($P_{\text{interaction}} = 0.04$) were more pronounced among young adults than in older adults.

Table 6.5 IRRs between the individual CVH metrics and IHD prevalence, stratified by sex.

Metrics	Population	Crude IRR (95% CI)	*P*	Adjusted IRR* (95% CI)	*P*	$P_{interaction}$
Smoking	Males	1.84 (1.21-2.79)	0.01	1.12 (0.77-1.63)	0.56	0.49
	Females	1.30 (0.78-2.18)	0.31	1.41 (0.79-2.51)	0.24	
High BMI	Males	1.93 (1.26-2.97)	<0.01	1.32 (0.91-1.90)	0.14	0.14
	Females	2.13 (1.27-3.58)	0.01	1.51 (0.85-2.71)	0.15	
Physical inactivity	Males	3.57 (1.94-6.55)	<0.01	1.84 (1.00-3.39)	0.048	0.38
	Females	9.47 (1.88-47.73)	0.01	3.99 (0.79-20.12)	0.09	
Unhealthy dietary pattern	Males	0.42 (0.17-1.06)	0.06	1.13 (0.52-2.43)	0.76	0.82
	Females	1.24 (0.50-3.07)	0.64	1.33 (0.53-3.29)	0.54	
Elevated TC	Males	2.56 (1.66-3.95)	<0.01	1.53 (1.04-2.25)	0.03	0.85
	Females	5.22 (2.07-13.18)	<0.01	1.70 (0.65-4.42)	0.28	
Elevated BP	Males	1.62 (1.07-2.45)	0.02	0.81 (0.57-1.16)	0.25	0.89
	Females	3.46 (1.93-6.21)	<0.01	0.85 (0.43-1.69)	0.63	
Elevated FPG	Males	2.56 (1.84-3.55)	<0.01	1.20 (0.85-1.67)	0.29	1.00
	Females	2.98 (1.66-5.34)	<0.01	1.20 (0.56-2.57)	0.64	

*Adjusted for age (continuous), education attainment, income, and residence region.

Abbreviations: IRR, incidence rate ratio; CI, confidence interval; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

Table 6.6 IRRs between the individual CVH metrics and IHD prevalence, stratified by age.

Metrics	Population	Crude IRR (95% CI)	*P*	Adjusted IRR* (95% CI)	*P*	$P_{interaction}$
Smoking	Young adults	1.67 (0.89-3.14)	0.11	1.10 (0.55-2.18)	0.78	0.48
	Older adults	1.35 (0.95-1.92)	0.09	1.22 (0.84-1.75)	0.29	
High BMI	Young adults	4.42 (1.64-11.92)	< 0.01	2.28 (0.84-6.16)	0.10	0.01
	Older adults	1.07 (0.78-1.47)	0.66	1.15 (0.86-1.52)	0.34	
Physical inactivity	Young adults	7.08 (1.56-32.16)	0.01	4.34 (0.87-21.55)	0.07	0.03
	Older adults	1.91 (1.17-3.12)	0.01	1.63 (1.01-2.64)	0.046	
Unhealthy dietary pattern	Young adults	0.93 (0.21-4.11)	0.93	0.91 (0.21-3.95)	0.90	0.31
	Older adults	1.27 (0.66-2.44)	0.47	1.26 (0.67-2.37)	0.47	
Elevated TC	Young adults	2.69 (1.27-5.66)	0.01	1.12 (0.51-2.48)	0.77	0.51
	Older adults	1.47 (0.98-2.21)	0.06	1.67 (1.11-2.51)	0.02	
Elevated BP	Young adults	3.69 (1.92-7.12)	< 0.01	1.56 (0.67-3.62)	0.29	< 0.01
	Older adults	0.78 (0.50-1.22)	0.28	0.61 (0.40-0.92)	0.02	
Elevated FPG	Young adults	3.60 (1.77-7.30)	< 0.01	1.72 (0.77-3.83)	0.18	0.04
	Older adults	1.29 (0.92-1.80)	0.14	1.05 (0.74-1.47)	0.79	

*Adjusted for age (continuous), sex, education attainment, income, and residence region.
Abbreviations: IRR, incidence rate ratio; CI, confidence interval; BMI, body mass index; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose.

The sex and age-specific adjusted PAFs were displayed in **Figure 6.2** and **6.3**, respectively. Among males, physical inactivity and elevated TC contributed to 37.6% and 24.8% of IHD burden (**Figure 6.2**). Elevated TC and physical inactivity contributed to 34.4% and 34.3% of IHD burden (**Figure 6.3**). None of the seven metrics was a significant contributor to IHD in females and younger adults.

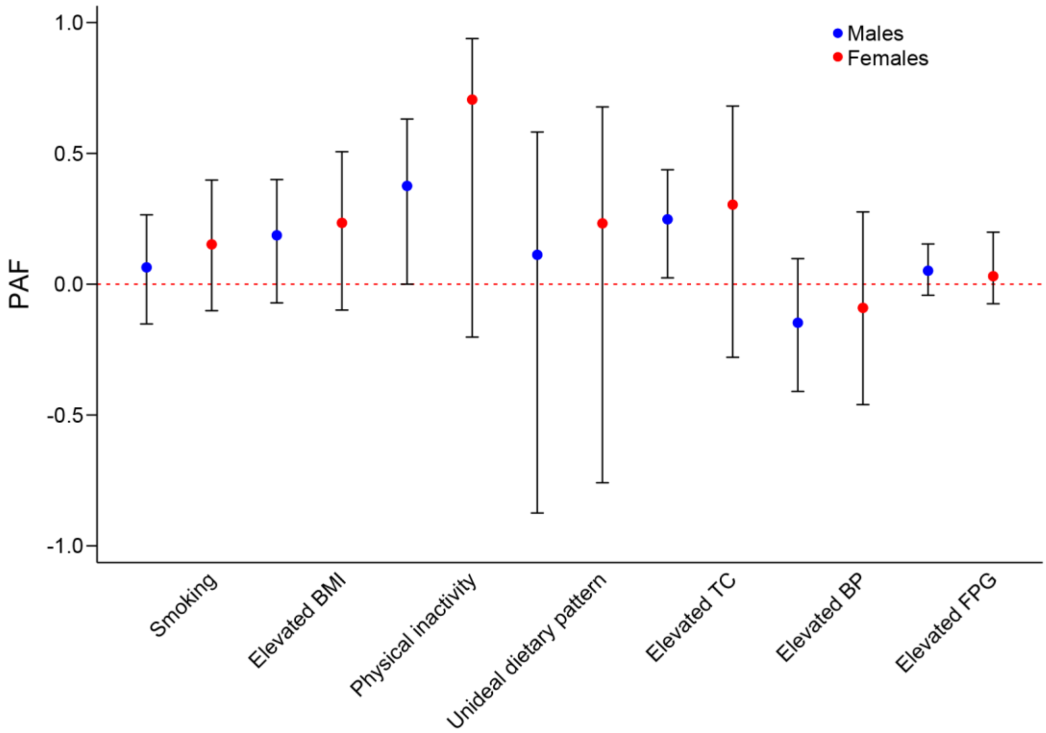

Figure 6.2 Adjusted PAFs of the CVH metrics to IHD prevalence, stratified by sex. Abbreviations: PAF, population attributable fraction; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CVH, cardiovascular health; IHD, ischemic heart disease.

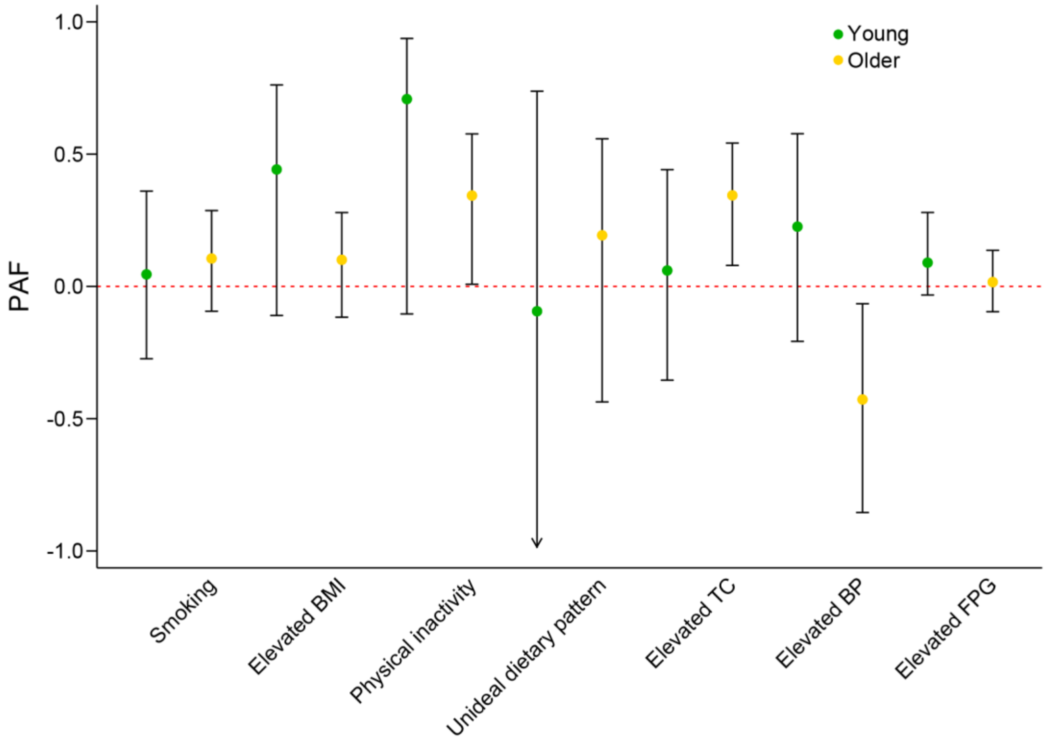

Figure 6.3 Adjusted PAFs of the CVH metrics to IHD prevalence, stratified by age. Abbreviations: PAF, population attributable fraction; TC, total cholesterol; BP, blood pressure; FPG, fasting plasma glucose; CVH, cardiovascular health; IHD, ischemic heart disease.

Sex- and age-specific associations between the number of ideal CVH metrics and IHD prevalence

We explored the association between the number of ideal CVH metrics and IHD prevalence based on 7002 participants who have no missing data on the seven metrics and the crude and adjusted ORs were shown in **Table 6.6**. We observed a negative association between the number of ideal CVH metrics and IHD prevalence in all sex and age subpopulations. Among females and young adults, we noticed a 59% (OR, 0.41; 95% CI, 0.19-0.88) and a 65% (OR, 0.35; 95% CI, 0.15-0.83) reductions in the odds of IHD prevalence for those with the intermediate CVH status and none of those with the ideal CVH status had self-reported IHD. For males and older adults, we observed non-significant reductions in the odds of IHD prevalence for those with the intermediate and ideal CVH. In addition, one more ideal CVH metric was associated with 11-31% reduced IHD prevalence while the association failed to reach a significant level for males and older adults. The analyses of interaction terms indicated that the impacts of the overall CVH status on IHD prevalence were similar among the four subgroups.

Table 6.7 ORs between the number of ideal metrics and IHD prevalence, stratified by sex and age.

Participants	Ideal Metrics Number	IHD cases/Participants	Crude OR (95% CI)	*P*	Adjusted* OR (95% CI)	*P*
Males	0-2	150/1741	Reference	NA	Reference	NA
	3-4	44/1147	0.34 (0.21-0.56)	< 0.01	0.65 (0.42-1.01)	0.06
	5-7	4/285	0.06 (0.01-0.51)	0.01	0.47 (0.05-4.30)	0.50
	One more ideal metric	NA	0.61 (0.53-0.70)	< 0.01	0.86 (0.73-1.02)	0.09
Females	0-2	99/1601	Reference	NA	Reference	NA
	3-4	29/1639	0.22 (0.11-0.45)	< 0.01	0.41 (0.19-0.88)	0.02
	5-7	0/589	NA	NA	NA	NA
	One more ideal metric	NA	0.52 (0.45-0.60)	< 0.01	0.73 (0.59-0.91)	0.01
Young	0-2	54/1708	Reference	NA	Reference	NA
	3-4	15/2028	0.18 (0.09-0.37)	< 0.01	0.35 (0.15-0.83)	0.02
	5-7	0/792	NA	NA	NA	NA
	One more ideal metric	NA	0.49 (0.40-0.60)	< 0.01	0.69 (0.52-0.91)	0.01
Older	0-2	195/1634	Reference	NA	Reference	NA
	3-4	58/758	0.61 (0.39-0.95)	0.03	0.68 (0.44-1.03)	0.07
	5-7	4/82	0.35 (0.04-2.91)	0.32	0.55 (0.06-5.09)	0.59
	One more ideal metric	NA	0.83 (0.71-0.97)	0.02	0.89 (0.76-1.05)	0.17

*Adjusted for age (continuous), sex, education attainment, income, and residence region.
Abbreviations: IHD, ischemic heart disease; OR, odds ratio; CI, confidence interval; NA, not applicable.

Discussion

By analyzing the nationally representative survey, we did not reveal the sexual variations in the strength of seven metrics and IHD prevalence. Our results demonstrated that the impacts of high BMI, physical inactivity, elevated BP, and elevated FPG were more apparent in young adults than in older adults. The association between ideal metrics number and IHD prevalence are similar among the four subgroups.

Although we found physical inactivity and elevated TC were significant IHD risk factors and contributors for only males, we did not reveal the differences in the IHD association strengths for all the metrics between men and women. However, a few recent meta-analyses have suggested the possible sex disparities in the effect sizes between the CVH metrics and IHD. [197, 199, 213] It appears that smoking and diabetes have a more potent influence on CHD risk in women whereas [199, 213] elevated TC has a more adverse effect on men. [197] We observed that physical inactivity and elevated TC were significant IHD risk factors for older adults instead of young adults. While the findings of interaction terms did not further support the possible age variations. Instead, the interaction term analyses implied the increased BMI, physical inactivity, elevated BP and elevated FPG are associated with greater prevalence in young adults than older adults are. To our knowledge, no meta-analysis explored the age disparities between the CVH metrics and IHD risk. The decreasing effects of high BMI, [17] elevated BP, [17, 191] and elevated FPG [17, 214] with age were also noticed in a few observational studies. The age variations in the physical inactivity-IHD relationship were unclear. However, a study has noted the association between physical inactivity and overall CVD was stronger among young adults. [215] The different study designs (cohort versus cross-sectional) and outcomes (incidence/mortality versus prevalence) may partly explain the inconsistent findings. The secondary prevention in IHD patients could partly explain why some metrics loss significance in some subgroups. However, we can still observe the significant differences in distribution of CVH metrics, except for dietary pattern, among IHD and non-IHD participants, and some factors of secondary prevention, like medicines for diabetes and hypertension, were not evaluated in our study. Therefore, more studies should focus on the secondary prevention of IHD in sex- and age-specific populations. Given the inconclusive findings, more large-scale prospective studies are warranted.

We observed that an increasing number of ideal metrics was associated with reduced IHD prevalence and the negative association was also found in other studies. [5, 30] The very few IHD cases in those with the ideal CVH status, especially in females and young adults, suggested the apparent protective effect of the CVH status. The strengths of association were similar among the four groups, which indicate the disparities in IHD prevalence was less likely to be explained by the

CVH metrics. A number of other factors, including education, [216] income, [217] and knowledge/awareness of IHD [218] were found to be associated with IHD prevalence and whether they could explain the sex and age disparities in IHD prevalence still need further explorations.

Our study has several strengths: we firstly explored sex and age variances in the associations between the CVH metrics and IHD prevalence in Australian adults; we have drawn our conclusions based on a nationally representative sample; we adjusted some factors that could be potential confounders. Our study also has several limitations. Firstly, the IHD status was self-reported and it may lead to overestimation or underestimation of IHD prevalence. Previous studies have explored the accuracy of self-reported myocardial infarction, a common type of IHD, and they observed moderate [186, 187] or substantial [185, 219] agreement between self-reported questionnaire and medical record data. We need studies with medical record diagnosed IHD to focus on the topic. Secondly, demographic factors, smoking, physical activity, and dietary pattern were self-reported, and they may not be wholly accurate. Thirdly, we could not explore the sex and age variations in the associations between the CVH metrics and IHD incidence or mortality as our study was a cross-sectional study. Fourthly, we may still suffer from the selection bias even though, as recommended by the ABS, we applied biomedical weights. We noticed the differences for some demographic factors and CVH metrics between participants and non-participants (**Table 4.2**). Fifthly, we modified the classifications of CVH metrics compared to the AHA's guideline due to the dataset structure. For instance, we only included fruits and vegetables as dietary components as other dietary components were not available in AHS. Sixthly, 17.7% of the total participants were self-reported CVD other than IHD, and they were classified as non-IHD group in our study. It may underestimate the associations between Life's Simple 7 and IHD prevalence.

Conclusions

In summary, we noticed the associations between high BMI, physical inactivity, elevated BP, and elevated FPG and IHD prevalence were greater in young adults relative to that in older adults. No sex differences were observed between the individual CVH metrics and IHD prevalence. The impacts of the ideal metrics number on IHD prevalence were similar among the four subgroups. Further large-scale prospective studies are warranted to confirm the possible sex and age disparities.

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Conflicts of Interest: The authors declare no conflict of interest.

Chapter 7 – Discussion

Key findings of the thesis

Chapter 2 evaluated the proportions of ideal status for the seven CVH metrics and percentages of the overall poor and ideal CVH status, defined by the number of ideal metrics, in adults worldwide using a systematic review and meta-analysis. As a result, the proportion of ideal status was high for some metrics (eg, smoking, FPG), but was low for other metrics (eg, dietary pattern, BP). In addition, we observed the alarming high (> 30%) overall poor CVH status and relatively low (< 20%) overall ideal CVH status and is generally in agreement with a previous systematic review. [11] Females and young adults (< 60 years) generally have better CVH status compared to males and older adults (≥ 60 years). Our findings also indicate the unsatisfactory CVH status was prevalent in nearly all areas and very few studies have conducted in Oceania and Africa. Although we noticed the improvement of the CVH over study time, more studies are needed to monitor the trend.

Chapter 3 summarized the findings on the separate and combined effects of the CVH metrics and CVD related events using a systematic review. The results indicated a greater number of ideal metrics was associated with a substantial reduction in CVD risk and two previous systematic reviews suggested similar results. [13, 14] There existed inconsistent findings regarding the effects of the seven CVH metrics on the risk of various CVD events. Furthermore, few studies have explored the sex and age variances in the magnitude of the association between separate and combined effects of CVH metrics and CVD risk.

Chapter 4 explored the CVH status in Australian adults using the core sample of the 2011-2012 AHS, which is a nationally representative survey. We noticed the overall CVH status was poor in the overall population and sex/age subgroups. The proportion of ideal status was highest for FPG and lowest for dietary pattern. Compared to males and older adults, females and young/middle-aged adults appeared to have higher proportions of ideal status for most CVH metrics, higher prevalence of the overall ideal CVH status, and lower prevalence of the overall poor CVH status.

Chapter 5 illustrated the separate and combined associations between the CVH status and CVD prevalence in the overall and sex/age subpopulations in Australian adults. Smoking, high BMI, elevated BP, elevated TC, elevated FPG, and physical inactivity were significant risk factors and contributors of CVD prevalence in the overall population. High BMI, elevated TC, elevated BP, and elevated FPG were significant CVD risk factors and contributors for males while smoking, high BMI, elevated BP, and elevated FPG were significant for females. Smoking was the only one significant risk factor and contributor of CVD prevalence in young adults. High BMI, elevated BP, and elevated FPG were independently associated with CVD prevalence in middle-aged adults. High

BMI, physical inactivity, and elevated FPG were significant risk factors and contributors of CVD prevalence in older adults. The analyses of interaction terms indicated that the associations between non-ideal status of TC/BP and CVD prevalence were more apparent in males than in females. The association between physical inactivity and CVD prevalence was more obvious in older adults. The unhealthy dietary pattern has a greater impact on young adults. The increased ideal number of the CVH metrics was associated with CVD reduction in overall and most age/sex subpopulations and the association was more obvious for males than females.

Chapter 6 studied the separate and combined associations between the CVH status and IHD prevalence in the overall and sex/age subpopulations in Australian adults. Physical inactivity, elevated BMI, and elevated TC were significant IHD risk factors and contributors in the overall population. Physical inactivity and non-ideal TC were significant IHD risk factors and contributors for males and older adults. None of the seven metrics was a significant IHD risk factor and contributor for females and young adults. The analyses of interaction terms demonstrated that the associations between elevated BMI, physical inactivity and non-ideal BP/FPG and IHD prevalence were more apparent in young adults. The number of ideal metrics was inversely associated with IHD prevalence in the overall and subgroups while the strengths of impact in IHD prevalence reduction were similar among the four sex/age groups.

Implications of the findings

Our study highlighted the importance of primordial prevention in reducing the population-wide CVD burden. Our findings indicated that the prevalence of the overall ideal CVH status was extremely low in adults from worldwide and Australia. Moreover, the findings indicated a graded association between the number of ideal metrics and the risk of CVD and IHD. The situation reminded the policy makers, health professionals, and researchers to not only focus on those already at highest risk of CVD/IHD (the high-risk strategy) but also pay attention to the promotion and improvement of the cardiovascular risk distribution in the whole population (the population-wide strategy). A number of population-wide primordial prevention strategies, including smoking cessation, salt reduction, weight loss, and physical activity promotion, were shown to reduce the risk of CVD. Several systematic reviews and meta-analysis documented the smoke-free legislations could substantially reduce the CVD events in many countries. [220-222] In Australia, there are national and state/territory legislations in restricting smoking in indoor environments, such as public transit, shopping malls, schools and cinemas. [223] However, the regulations for managing smoking in outdoor areas varied across regions. [223] Moreover, the regulations of electronic cigarette are very limited. [224] Recent studies documented the effectiveness of population-wide salt reduction programs in lowering the CVD risk. [225, 226] A number of programs have conducted to reduce the salt intake in

Australia. [227] However, there is no campaign to influence consumer behavior regarding salt and no mechanism to monitor the changes in salt intake national wide. [227] It has been suggested that a population-wide weight loss was associated with a marked reduction in CVD mortality in Cuba. [228] A few community-based weight loss programs have initiated in Australia; [229, 230] however, there is no national-level strategies or programs to manage the weight loss. The intervention of increased physical activity and reduced sedentary time could substantially lower the CVD burden. [231, 232] An Australian interventional study proved that reduced sitting time and increased physical activity in the workplace could dramatically improve the cardiometabolic biomarkers. [233] Hence, interventional programs of physical activity should be advocated and implemented in the national level. Several studies have proposed the consumption of fish oil [234] and mobile health devices [235] as potential CVD prevention strategies. We need more studies to explore their population-wide effects in primordial prevention of CVD.

Another striking implication is the sex and age disparities in the distribution of CVH metrics and their associations and contributions to CVD/IHD risk. Previous studies suggested that males and older adults have significant higher risk of CVD mortality as compared to their females and young adults counterparts. [236, 237] Additionally, the sex and age differences in the prevalence of modifiable cardiovascular risk factors has been observed. [212, 238] Therefore, we hypothesized that there may be sex and age variances in the distribution of CVH metrics, and those variances could explain the gaps in CVD or IHD risk. As a result, the females and young adults have marked higher prevalence of ideal status for most CVH metrics and have better overall CVH status compared to their males and older counterparts in worldwide (chapter 2) and Australia (chapter 4). Very few studies have focused on the sex and age differences in the associations between CVH metrics and CVD, including IHD, risk (chapter 3). In males, the non-ideal TC and BP have greater association and contribution to CVD prevalence, and the overall CVH status has stronger association to CVD prevalence. However, the separate and combined effects of Life's Simple 7 and CVD prevalence were similar among the age subgroups (chapter 5.2). The CVH metrics have similar associations with IHD prevalence in both sex, and some of them even have stronger associations with IHD prevalence among young adults. There is no sex and age differences in the association between the overall CVH status and IHD prevalence. Thus, the CVH metrics could not explain the sex and age differences in the risk of IHD prevalence (chapter 6.2). Giving the higher prevalence and stronger CVD associations of non-ideal TC and BP in males, the two metrics should be drivers of sex differences in CVD prevalence. Older adults have higher rate of physical inactivity, and the magnitude of association between physical inactivity and CVD prevalence was greater in older adults. Thus, we should pay more attention to increase the physical activity level in older adults. The current evidence demonstrated that the CVH metrics could not explain the sex and age variances in IHD prevalence. More large-scale cohort and interventional studies are warranted to explore the topic and closing the gaps of CVD and IHD risk across the sex and age subgroups.

Our study indicated Life's Simple 7 could be a useful tool to estimate and monitor the CVH status in Australia. Life's Simple 7 have several advantages over other established CVD risk stratification tools. Firstly, Life's Simple 7 could evaluate the CVH status in broader population. It could provide the information on CVH status for all adults and children. [7] However, the general cardiovascular risk profile [8] and CHD prediction model, [9] developed by the Framingham Heart Study, could only calculate the future risk of CVD and CHD among participants aged ≥ 30 years and 30-74 years, respectively. The guideline for absolute CVD risk, established by the Australian National Vascular Disease Prevention Alliance, could only evaluate the CVD risk for adults aged 45 years or over. [10] Secondly, Life's Simple 7 considers more CVD risk factors. For example, it included five dietary components; [7] however, other tools failed to consider dietary pattern. [8-10] Thirdly, Life's Simple 7 is more easily to measure. It only considered the status of seven metrics and the number of ideal metrics. [7] The other tools [8-10] need to calculate a score based on the combinations of several factors, and it may difficult for some participants. There are some limitations for Life's Simple 7 as well. For instance, it does not included sex and age as predictors and it does not provide individualized score for future CVD risk. [7] There are a few Australian studies, apart from ours, that used Life's Simple 7 to evaluate the CVH status in children [239] and adults. [111, 239] Life's Simple 7 should be applied in larger Australian samples to monitor the CVH status over time and its association with CVD mortality and incidence.

Our findings indicated the significance of secondary prevention of CVD and IHD in Australia. We observed that the associations between some CVH metrics and CVD/IHD prevalence were attenuated in overall and sex/age subgroups. It could be possible that the CVD and IHD patients received medication or taken some lifestyle modifications after diagnosed with the diseases. However, we still observed the significant differences in the distribution of CVH metrics among patients and non-patients. In addition, the AHS lacked a few key indicators of secondary prevention, such as medications for BP and diabetes. Therefore, our study failed to answer the performance of CVD/IHD clinical management. The Australian government has realized the needs of secondary prevention and worked out a blueprint of reform for secondary prevention of CHD. [240] Recently, a few studies have evaluated the performance of CVD secondary prevention. [3, 241] A cross-sectional study in South Australia reported the poor situation of secondary prevention among CVD patients. [241] It indicated that only 30% of CVD patients have adequate fruits and vegetables consumption and 31% of participants have adequate physical activity. [241] A cohort study in New South Wales suggested the possible socioeconomic variations in CVD secondary prevention. [3]

Among CVD patients, those with low education level have greater risk of developing major CVD events than those with high education level and the variance was more apparent in males. [3] To the best of our knowledge, there are very few studies on the clinical management of CVD and IHD patients from the national level. Therefore, monitoring and improving the clinical management of CVD and IHD patients with special attention to the disadvantaged persons, such as those with low education level, should be one of the priorities of Australia.

Strengths of the study

First, the two systematic reviews summarised the recent findings in the CVH status and its association with CVD/IHD risk in adults worldwide, which provided reliable evidence for the policy makers and researchers.

Second, to the best of our knowledge, we firstly evaluated the CVH status and its association with CVD and IHD prevalence in Australian adults using a nationally representative survey. The findings are crucial for prioritize the CVD and IHD prevention strategies and promote the CVH status in Australian adults.

Limitations of the study

For the systematic review and meta-analysis on the CVH status worldwide, it suffered from significant heterogeneity, and age, sex, study period and regions could not fully explain the heterogeneity. In addition, we could not compare the CVH status of Australia with other regions accurately because of the very limited studies in Australia.

For the systematic review on the CVH status with CVD/IHD risk, as most studies could not strictly follow the AHA's definition of Life's Simple 7, and it may bias the true association between Life's Simple 7 and CVD-related events. Although there are several studies focused on the risk factors of some relative rare CVD subtypes, like HF [242] and cardiac arrest, [243] there existed significant regional variances and the separate and combined effects of CVH on their risks were not well documented, especially for sex and age subgroups.

There are several drawbacks for analyses based on the 2011-2012 AHS. Firstly, the 2011-2012 AHS is a cross-sectional study, and we could not establish the causal relationship between Life's Simple 7 and incidence/mortality of CVD or IHD. It could also induce reverse causality as those diagnosed with CVD/IHD may take lifestyle modifications or medicines, and it may bias the associations between CVH metrics and CVD/IHD prevalence. Secondly, although we used the biomedical weight to make our findings nationally representative, we may still suffering from the risk of selection bias as we observed the differences in distribution of some demographic and CVH metrics among participants (those with TC and FPG) and non-participants (those without TC and

FPG) (**Table 4.2**). Thirdly, we did not explore the associations of other possible factors, like socioeconomic and genetic factors, with risk of CVD or IHD. Fourthly, we modified the classification of several CVH metrics due to dataset structure of the AHS. For example, we assessed dietary pattern based on consumption of fruits and vegetables as other dietary components outlined by the AHA were not existed in the AHS. The modifications may partially explain why the dietary pattern was not associated with CVD and IHD prevalence in the overall and sex/age specific population. Fifthly, the CVD and IHD prevalence in our study were self-reported, and they may not entirely accurate. Some other metrics and covariates were also self-reported. Sixthly, we used poisson and logistic regression analyses in our study as the log-binomial regression analyses were not allowed by the system of ABS. It may overestimate the effect sizes. Seventhly, we could not explore the associations between the CVH metrics and some types of CVDs as they were not separately listed as conditions and/or have very limited cases. Eighthly, we did not compare the CVH status and the strengths of its association with CVD and IHD prevalence between non-indigenous and indigenous Australians as indigenous Australians were not included in the AHS. Ninthly, as very few studies explored the associations between CVH metrics and CVD/IHD prevalence, it is difficult to make direct comparisons between our findings with others. In addition, the AHS only collected one single measurement of the CVH metrics. We could neither monitor the CVH status over time nor explore the cumulative impacts of the CVH metrics on CVD/IHD incidence and/or mortality.

Directions for future studies

As we noticed, very few studies have used Life's Simple 7 to measure the CVH status and explore its association with future CVD mortality and incidence in Australian adults, including in the indigenous Australian adults. More studies with larger sample size are needed to focus on these topics.

As most studies have one single measurement of the CVH metrics, more studies with multiple measurements of CVH metrics are warranted. It will not only facilitate the monitor of the CVH status over time but also explore the cumulative effects of the CVH status on mortality and incidence of CVD.

More studies should pay attention to the effectiveness of population-based intervention strategies to the prevention of CVD. Moreover, the combined effects multiple interventions were still unclear and they need further explorations.

The interactions between the CVH metrics and several other factors, such as socioeconomic and genetic factors, on the risk of CVD were largely unknown, and we need more studies on this topic.

We classified participants into three CVH categories (poor CVH: 0-2 ideal metrics; intermediate CVH: 3-4 ideal metrics; ideal CVH: 5-7 ideal metrics), and explored the associations between CVH categories and CVD/IHD prevalence. Using poor CVH status as reference, moderate and ideal CVH status was associated with a 33% and a 66% reduced CVD prevalence. Using poor CVH status as reference, moderate and ideal CVH status was associated with a 45% and a 78% reduced IHD prevalence. The graded association was also noticed in sex and age subgroups. However, we assumed the CVH status was similar within categories. In future studies with larger sample size, we could divide CVH status into more categories, for example eight categories, and evaluate the association between CVH status and CVD risk in more details.

Conclusions

In summary, the overall CVH status was poor among adults in worldwide and Australia. The proportions of ideal status were extremely low for metrics like dietary pattern and physical activity. Both the meta-analysis and the AHS indicated females and young adults have better CVH status than did males and older/middle-aged adults.

The systematic review revealed the negative association between number of the ideal CVH metrics and risk of multiple CVD outcomes. It produced mixed findings on the associations between individual metrics and CVD related outcomes, and very few studies focused on the sex and age differences in the magnitude of associations between Life’s Simple 7 and CVD risk. The AHS suggested that smoking, high BMI, physical inactivity, elevated TC, elevated BP, and elevated FPG were significant CVD risk factors and contributors in the overall population. High BMI, physical inactivity, and elevated TC were significant IHD risk factors and contributors in the overall population. There existed sex and age variances in the separate and combined associations between the CVH metrics and CVD/IHD prevalence in Australian adults.

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Appendix

The ethical approvals of the thesis.

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

School of Medicine

The University of Queensland
Mayne Medical School
Herston Road
Herston Qld 4006 Australia

School of Medicine Approval Form for Research Involving Humans Including Behavioural Research

for Honours, MPhil & PhD Students in the School of Medicine

Chief Investigator (student)	Yang Peng
Project Title	Risk factors for cardiovascular and renal diseases in Australia and United States population
Supervisor(s)	Zhiqiang Wang
Co-Investigator(s)	Bin Dong
Research Centre/Institute/School	School of Medicine / Centre for Chronic Disease
SOM Clearance Number	**2016-SOMILRE-0161**
Date of Issue	6 March 2016
Date of Expiry	6 March 2018

Comments:

Low risk research and previous UQ approval #2015001731.

UQ School of Medicine Low Risk Ethical Review Committee

This project complies with the provisions contained in the National Statement on Ethical Conduct in Human Research (complies with the regulations governing research involving humans) and UQ ethical paragraphs concerning low risk research.

UQ School of Medicine Low Risk Ethical Review Committee Representative

Associate Professor Diann Eley

Diann Eley

6 March 2016

Signed

Date

THE UNIVERSITY OF QUEENSLAND

Sub-Committee Human Research Ethics Approval

Project Title:	Risk factors for cardiovascular and renal diseases in Australia and United States population - 07/02/2018 AMENDMENT
Chief Investigator:	Mr Yang Peng
Supervisor:	Zhiqiang Wang
Co-Investigator(s):	Bin Dong
School(s):	School of Medicine, UQ
Approval Number:	2018000244
Granting Agency/Degree:	PhD
Duration:	1st March 2020

Comments/Conditions:

Amendment 07/02/2018

- Extension of Project to 1st March 2020

Original Application approved by School of Medicine, Clearance No: 2016-SOMILRE-0161

Note: if this approval is for amendments to an already approved protocol for which a UQ Clinical Trials Protection/Insurance Form was originally submitted, then the researchers must directly notify the UQ Insurance Office of any changes to that Form and Participant Information Sheets & Consent Forms as a result of the amendments, before action.

Name of responsible Sub-Committee:
University of Queensland Medicine, Low & Negligible Risk Ethics Sub-Committee

This project complies with the provisions contained in the *National Statement on Ethical Conduct in Human Research* and complies with the regulations governing experimentation on humans.

Name of Ethics Sub-Committee representative:
Associate Professor Diann Eley
Chairperson
University of Queensland Medicine, Low & Negligible Risk Ethics Sub-Committee

Signature Diann Eley Date **08/02/2018**